Supporting Information for

Catalytic Asymmetric Synthesis of Diphenylbutazone Analogues

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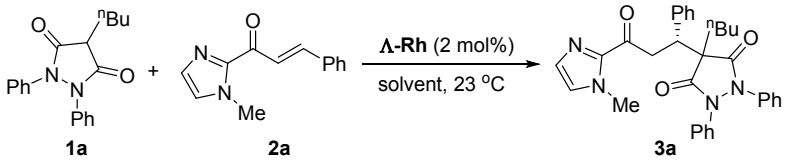
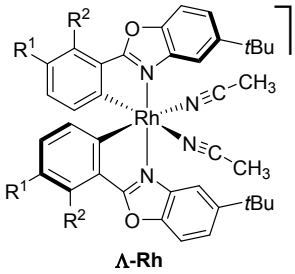
I General Information

All reactions were performed in Schlenk tubes at room temperature using oven-dried glassware. Commercially obtained reagents were used without further purification, unless otherwise noted. Dry 1,2-dichloroethane (DCE) and methyl tert-butyl ether (MTBE) were obtained from solvent distillation machine (Vigor VSPS-5) and stored under argon over 4 Å type molecular sieves. Chloroform was distilled over P_2O_5 and stored over 3 Å type molecular sieves. THF and toluene were distilled freshly before use over sodium and benzophenone. Dichloromethane (DCM) was distilled from CaH_2. Methanol was used without further purification. Reactions were checked by TLC analysis and plates were visualized with short-wave UV light (254 nm). The ^{1}H, ^{13}C NMR and ^{19}F spectra were obtained in $CDCl_3$ using a Bruker-BioSpin AVANCE III HD NMR spectrometer at 400 and 100 MHz， respectively. Chemical shifts are reported in parts per million (δ value) calibrated against the residual solvent peak. Signal patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in hertz (Hz). HPLC analyses of the compounds were done using chiralcel IA-IF columns and chiralcel AD-H, AS-H, OJ-H and OD-H columns using hexane and isopropanol as eluent. The infrared spectra were recorded on a Bruker VERTEX 70 IR spectrometer as KBr pellets, with absorption reported in cm^{-1}. High-resolution mass spectra were recorded on a Bruker Impact II UHR TOF LC/MS Mass Spectrometry. Crystal structure data were collected on a SuperNova, Dual, Cu at zero, Atlas diffractometer.

II Optimization of Reaction Conditions

STable 1. Optimization of the Reaction Conditions[a]





Λ-Rh

Λ-Rh	R^1	R^2
Λ-Rh1	H	H
Λ-Rh2	CF_3	H
Λ-Rh3	H	3,5-$(CH_3)_2C_6H_3$
Λ-Rh4	H	3,5-$(CF_3)_2C_6H_3$

entry	**Λ-Rh** (2 mol %)	solvent	time (h)	yield (%)[b]	ee(%)[c]
1	**Λ-Rh1** (2)	toluene	3	96	89
2	**Λ-Rh1**(2)	THF	1.5	96	97
3	**Λ-Rh1** (2)	DCM	1	95	97
4	**Λ-Rh1** (2)	CH_3OH	2	93	97
5	**Λ-Rh1** (2)	MTBE	3	93	96
6	**Λ-Rh1** (2)	$CHCl_3$	2	94	97

[a]Reaction conditions: **1a** (0.20 mmol), **2a** (0.1 mmol), **Λ-Rh1** (2 mol %), solvent (1 mL) at 23 °C under argon atmosphere. [b]Isolated yields. [c]Determined by chiral HPLC.

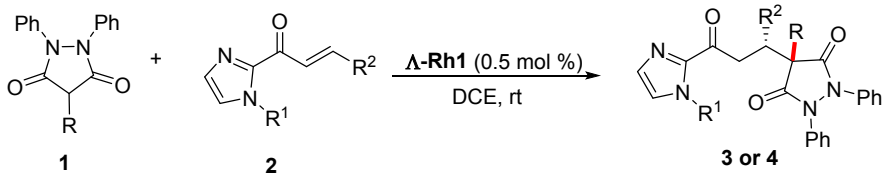
III Experimental Section

Λ-Rh1, Λ-Rh2, Λ-Rh2, Λ-Rh3 and Λ-Rh4 was prepared according to reported procedure.[1] α,β-unsaturated 2-acyl imidazoles[2] and Diphenylbutazone Analogues were synthesized according to reported procedures.[3-4]

Preparation of a stock solution of the catalyst Λ-Rh1 in DCE.

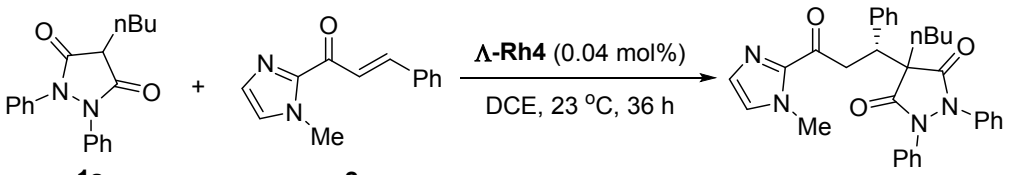
Stock solution of 2.0 mM:The chiral rhodium complex **Λ-Rh1** (8.3 mg, 10.0 μmol) was dissolved in freshly distilled DCE (5.0 mL).

General procedure for catalytic asymmetric synthesis of diphenylbutazone analogues.



To an oven-dried 25 mL Schlenk tube equipped with a stir bar, **Λ-Rh1** (0.5 mol %) (**Λ-Rh1** in DCE**;** 0.5 mL) was added along with *α,β*-unsaturated 2-acyl imidazole **2** (1 equiv., 0.2 mmol) and DCE (0.5 mL). After being stirred at room temperature for 5 min, diphenylbutazone **1** (2.0 equiv., 0.40 mmol) was added. The reaction was stirring at room temperature until consumption of the 2-acyl imidazole (monitored by TLC). The reaction mixture was concentrated and directly purified by silica gel column chromatography (with ethyl acetate-petroleum ether as the eluent) to afford the desired products **3** or **4**.

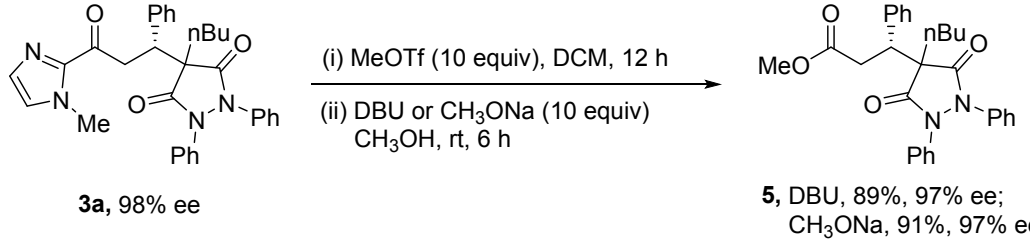
General procedure for gram-scale experiments with lower catalyst loading.



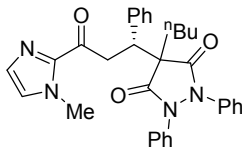
To an oven-dried 50 mL Schlenk tube equipped with a stir bar, **Λ-Rh4** (1.26 mg, 0.04 mol%) was added along with *α,β*-unsaturated 2-acyl imidazole **2a** (0.8061 g, 3.80 mmol, 1.0 equiv) and DCE (19 mL). After being stirred at room temperature for 5 min, diphenylbutazone **1a** (2.34 g, 7.60 mmol, 2.0 equiv) was added. The reaction was

stirring at room temperature until consumption of the 2-acyl imidazole as monitored by TLC for 36 h. The solution directly purified by silica gel column chromatography (EtOAc/Petroleum ether = 1:3) to afford **3a** (white solid, 1.92 g, 97% yield, 98% ee).

General procedure for synthetic transformation.

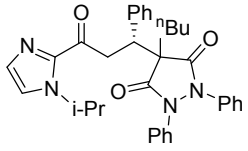


3a (52 mg, 0.10 mmol, 1.0 equiv) was added to a screw-cap tube followed by CH_2Cl_2 (2 mL). The solution was stirred at 0 ^oC and MeOTf (112 uL, 1.0 mmol, 10 equiv) was added dropwise. The solution was stirred at room temperature overnight, after which it was concentrated under reduced pressure. CH_3OH (2 ml) was added to the mixture, and then DBU (10 equiv) or CH_3ONa (10 equiv) was added to the solution. It's stirred at room temperature for an additional 6 h. The solution was quenched with saturated NH_4Cl (10 mL), and then the mixture was diluted with EtOAc (20 mL) and transferred to a separatory funnel. Brine (20 mL), and H_2O (15 ml) were added and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated on a rotary evaporator. The residue was purified by flash column chromatography to afford **5** (DBU as the base: 42 mg, 89% yield, 97% ee; CH_3ONa as the base: 43 mg, 91% yield, 97% ee).



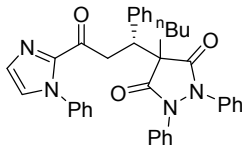
3a

White solid, m.p. 149.5-150.2 °C, 97 mg, 93% yield, 98% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, tr (major) = 20.43 min, tr (minor) = 16.17 min); $[\alpha]_D^{25}$ = +18.2 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.28 (m, 2H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.14-7.03 (m, 8H), 6.94 (t, *J* = 5.8 Hz, 3H), 6.73 (t, *J* = 7.3 Hz, 2H), 4.40-4.33 (m, 1H), 4.06-4.02 (m, 1H), 3.78 (s, 3H), 3.75-3.70 (m, 1H), 2.21-2.14 (m, 1H), 2.03-1.96 (m, 1H), 1.36-1.26 (m, 4H), 0.86 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.5, 172.2, 171.7, 143.0, 138.5, 135.0, 134.9, 129.2, 129.1, 128.7, 128.6, 128.4, 127.4, 126.9, 126.8, 126.7, 123.1, 123.0, 58.0, 46.2, 38.0, 35.9, 33.8, 27.2, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2959, 2927,1750, 1713, 1677, 1596, 1494, 1457, 1494, 1409, 1294, 758, 697. HRMS (ESI, *m*/*z*) calcd for $C_{32}H_{32}N_4NaO_3$ $[M+Na]^+$: 543.2367, found: 543.2367.



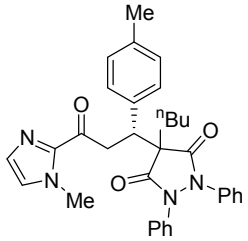
3b

Light yellow oil, 105 mg, 96% yield, 93% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 85/15, flow rate 1.0 mL/min, tr (major) = 16.51 min, tr (minor) = 14.08 min); $[\alpha]_D^{25}$ = +16.8 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.28-7.26 (m, 2H), 7.20-7.15 (m, 4H), 7.12-7.01 (m, 7H), 6.94 (t, *J* = 7.5 Hz, 2H), 6.74-6.71 (m, 2H), 5.28-5.21 (m, 1H), 4.36-4.29 (m, 1H), 4.08-4.05 (m, 1H), 3.81-3.76 (m, 1H), 2.22-1.98 (m, 2H), 1.34-1.19 (m, 10H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 189.4, 172.1, 171.6, 143.0, 138.2, 135.0, 134.9, 129.7, 129.6, 129.0, 128.9, 128.7, 128.6, 128.5, 127.5, 126.8, 126.7, 126.7, 125.4, 123.0, 123.0, 122.5, 58.0, 46.6, 38.3, 33.7, 27.2, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2960, 2928, 1751, 1715, 1675, 1596, 1494, 1397, 1296, 758, 699. HRMS (ESI, *m*/*z*) calcd for $C_{34}H_{36}N_4NaO_3$ $[M+Na]^+$: 571.2674, found: 571.2680.



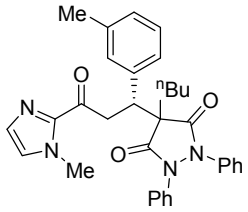
3c

Light yellow oil, 114 mg, 98% yield, 91% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, tr (major) = 12.09 min, tr (minor) = 10.86 min); $[\alpha]_D^{25}$ = +33.0 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31-7.24 (m, 6H), 7.20-7.00 (m, 10H), 6.94 (d, *J* = 7.6 Hz, 2H), 6.78 (d, *J* = 7.6 Hz, 2H), 6.70 (d, *J* = 7.6 Hz, 2H), 4.33-4.26 (m, 1H), 4.07-4.03 (m, 1H), 3.79-3.74 (m, 1H), 2.19-1.98 (m, 2H), 1.35-1.26 (m, 4H), 0.86 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.8, 172.2, 171.7, 142.3, 138.4, 135.0, 134.9, 129.6, 129.3, 128.7, 128.6, 128.4, 127.3, 126.7, 126.6, 123.1, 123.0, 58.0, 48.9, 46.6, 38.6, 33.8, 27.2, 23.5, 23.2, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2957, 2926, 1751, 1714, 1687, 1596, 1493, 1406, 1303, 758, 692. HRMS (ESI, *m*/*z*) calcd for $C_{37}H_{34}N_4NaO_3$ $[M+Na]^+$: 605.2516, found: 605.2523.



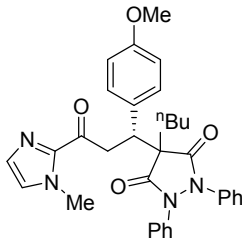
3d

White solid, m.p. 150.6-150.9 °C, 96 mg, 90% yield, 97% ee (HPLC: chiralpak AS-H column, 254 nm, hexane/isopropanol = 97/3, flow rate 1.0 mL/min, tr (major) = 38.91 min, tr (minor) = 32.15 min); $[\alpha]_D^{25}$ = +14.5 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21-7.04 (m, 9H), 6.97-6.88 (m, 5H), 6.73 (d, *J* = 7.8 Hz, 2H), 4.38-4.31 (m, 1H), 4.02-3.98 (m, 1H), 3.79 (s, 3H), 3.73-3.67 (m, 1H), 2.22-2.12 (m, 4H), 2.01-1.95 (m, 1H), 1.32-1.20 (m, 4H), 0.85 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.6, 172.4, 171.8, 143.1, 137.0, 135.2, 135.2, 135.1, 129.1, 129.0, 128.6, 128.4, 126.8, 126.5, 122.8, 58.1, 45.9, 38.0, 35.9, 33.7, 27.2, 22.8, 21.0, 13.7. IR (KBr): *v* (cm^{-1}) 2957, 2924, 2858, 1751, 1715, 1675, 1575, 1595, 1494, 1460, 1407, 1291, 758, 692. HRMS (ESI, *m*/*z*) calcd for $C_{33}H_{34}N_4NaO_3$ $[M+Na]^+$: 557.2522, found: 557.2523.



3e

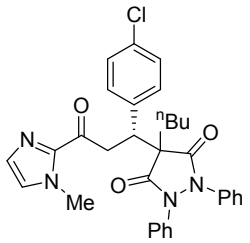
Light yellow oil, 102 mg, 95% yield, 96% ee (HPLC: chiralpak AS-H column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 8.10 min, tr (minor) = 7.11 min); $[\alpha]_D^{25}$ = +32.8 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.11-6.93 (m, 10H), 6.84 (d, *J* = 7.2 Hz, 4H), 6.66 (d, *J* = 7.6 Hz, 2H), 4.29-4.22 (m, 1H), 4.00-3.91 (m, 1H), 3.70 (s, 3H), 3.68-3.64 (m, 1H), 2.13-2.05 (m, 1H), 1.93-1.88 (m, 4H), 1.24-1.18 (m, 4H), 0.77 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.5, 172.3, 171.7, 143.0, 138.4, 138.1, 135.1, 135.0, 129.7, 129.1, 128.6, 128.5, 128.2, 128.1, 126.9, 126.5, 126.4, 126.3, 122.8, 122.7, 58.1, 46.0, 37.9, 35.9, 33.7, 27.2, 22.8, 21.2, 13.8. IR (KBr): *v* (cm^{-1}) 2958, 2925, 2859, 1751, 1714, 1675, 1595, 1493, 1460, 1408, 1290, 757, 692. HRMS (ESI, *m*/*z*) calcd for $C_{33}H_{34}N_4NaO_3$ $[M+Na]^+$: 557.2519, found: 557.2523.



3f

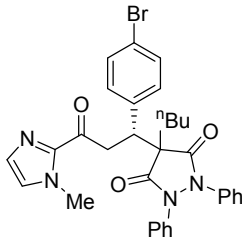
Light yellow solid, m.p. 151.3-151.5 °C, 106 mg, 96% yield, 91% ee (HPLC: chiralpak AS-H column, 254 nm, hexane/isopropanol = 95/5, flow rate 1.0 mL/min, tr (major) = 26.10 min, tr (minor) = 21.29 min); $[\alpha]_D^{25}$ = +12.2 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.22-7.18 (m, 4H), 7.15-7.03 (m, 5H), 6.99-6.93 (m, 3H), 6.78 (d, *J* = 7.6 Hz, 2H), 6.62 (d, *J* = 8.6 Hz, 2H), 4.37-4.30 (m, 1H), 4.02-3.98 (m, 1H), 3.78 (s, 3H), 3.69-3.64 (m, 1H), 3.67 (s, 3H), 2.18-2.12 (m, 1H), 2.01-1.95 (m, 1H), 1.32-1.24 (m, 4H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.6, 172.4, 171.8, 158.9, 143.1, 135.2, 135.1, 130.3, 130.2, 129.1, 128.6, 128.5, 126.9, 126.6, 122.8, 122.7, 113.7 58.2, 55.1, 45.6, 38.0, 35.9, 33.7, 27.2, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2957, 2927, 1751, 1714, 1675, 1595, 1513, 1492, 1460, 1289, 758, 692. HRMS (ESI, *m*/*z*)

calcd for $C_{33}H_{34}N_4NaO_4$ $[M+Na]^+$: 573.2468, found: 573.2472.



3g

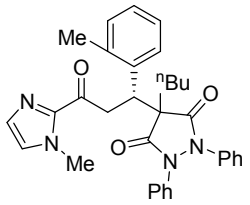
Light yellow solid, m.p. 158.3-158.6 °C,103 mg, 93% yield, 95% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, tr (major) = 18.92 min, tr (minor) = 13.71 min); $[\alpha]_D^{25}$ = +16.9 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.04 (m, 11H), 6.98-6.95 (m, 3H), 6.77 (d, *J* = 7.8 Hz, 2H), 4.41-4.34 (m, 1H), 4.04-4.00 (m, 1H), 3.79 (s, 3H), 3.69-3.63 (m, 1H), 2.19-2.13 (m, 1H), 2.01-1.95 (m, 1H), 1.33-1.30 (m, 4H), 0.85 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.2, 172.2, 171.6, 142.9, 136.9, 134.9, 133.4, 130.6, 129.3, 128.7, 128.7, 128.5, 127.1, 126.8, 126.7, 122.6, 122.5, 57.9, 45.7, 37.7, 35.9, 33.7, 27.1, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2958, 2925, 1752, 1714, 1673, 1595, 1493, 1460, 1141, 1291, 758, 693. HRMS (ESI, *m/z*) calcd for $C_{32}H_{31}ClN_4NaO_3$ $[M+Na]^+$: 577.1979, found: 577.1977.



3h

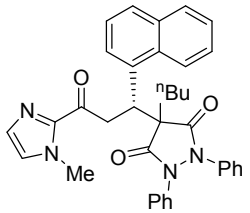
Light yellow solid, m.p. 157.2-157.7 °C, 117 mg, 98% yield, 97% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 10.12 min, tr (minor) = 7.91 min); $[\alpha]_D^{25}$ = +15.9 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.27-7.10 (m, 11H), 6.97 (d, *J* = 9.0 Hz, 3H), 6.77 (d, *J* = 8.1 Hz, 2H), 4.41-4.34 (m, 1H), 4.02-3.98 (m, 1H), 3.80 (s, 1H), 3.68-3.63 (m, 1H), 2.19-1.98 (m, 1H), 1.42-1.31 (m, 4H), 0.86 (t, *J* = 5.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.1, 172.2, 171.5, 142.9, 137.4, 135.0, 134.9, 131.5, 131.0, 129.3, 128.7, 128.7, 127.1, 126.8, 126.7, 122.6, 122.6, 121.6, 57.9, 45.7, 37.6, 36.0, 33.7, 27.1, 22.8, 13.7.

IR (KBr): *v* (cm^{-1}) 2957, 2926, 1751, 1714, 1675, 1595, 1491, 1460, 1410, 1290, 757, 692. HRMS (ESI, *m*/*z*) calcd for $C_{32}H_{31}BrN_4NaO_3$ $[M+Na]^+$: 621.1471, found: 621.1472.



3i

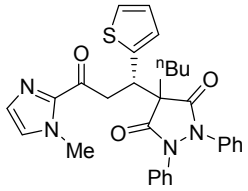
Light yellow oil, 98 mg, 92% yield, 94% ee (HPLC: chiralpak AD-H column, 254 nm, hexane/isopropanol = 65/35, flow rate 1.0 mL/min, tr (major) = 24.20 min, tr (minor) = 9.32 min); $[\alpha]_D^{25}$ = +15.7 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.39 (m, 1H), 7.26-7.23 (m, 3H), 7.13-6.96 (m, 9H), 6.90 (s, 1H), 6.75-6.72 (m, 2H), 4.40-4.08 (m, 2H), 3.79-3.73 (m, 1H), 3.74 (s, 3H), 2.37 (s, 3H), 2.24-1.97 (m, 2H), 1.42-1.26 (m, 4H), 0.86 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.7, 172.5, 171.8, 143.0, 138.0, 137.6, 135.2, 130.6, 129.1, 128.6, 125.9, 123.2, 123.0, 57.4, 40.9, 40.0, 35.8, 34.4, 27.0, 22.8, 20.0, 13.7. IR (KBr): *v* (cm^{-1}) 2925, 2856, 1751, 1714, 1677, 1595, 1493, 1460, 1409, 1292, 758, 692. HRMS (ESI, *m*/*z*) calcd for $C_{33}H_{34}N_4NaO_3$ $[M+Na]^+$: 557.2520, found: 557.2523.



3j

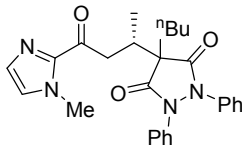
White solid, 102 mg, m.p. 146.5-146.9 °C, 89% yield, 94% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 22.60 min, tr (minor) = 9.83 min); $[\alpha]_D^{25}$ = +31.7 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.37 (d, *J* = 8.6 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.64-7.57 (m, 2H), 7.51-7.47 (m, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.20-7.07 (m, 5H), 7.00-6.87 (m, 6H), 6.52 (t, *J* = 7.4 Hz, 2H), 5.15-5.11 (m, 1H), 4.40-4.33 (m, 1H), 3.92-3.87 (m, 1H), 3.56 (s, 3H), 2.29-2.22 (m,1H), 2.11-2.04 (m, 1H), 1.32-1.25 (m, 4H), 0.85 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.3, 172.0, 171.8, 142.9, 135.4, 134.9, 134.8, 133.7, 132.1, 129.1, 128.6, 128.4, 128.1, 127.9, 126.7, 126.5, 126.4, 125.9, 125.2, 124.3,

122.7, 122.6, 57.6, 40.1, 39.2, 35.7, 34.1, 27.1, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2957, 2926, 1751, 1714, 1675, 1595, 1492, 1460, 1407, 1290, 779, 757, 692. HRMS (ESI, *m*/*z*) calcd for $C_{36}H_{34}N_4NaO_3$ $[M+Na]^+$: 593.2520, found: 593.2523.



3k

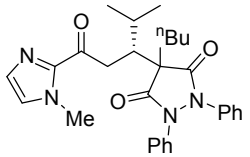
White solid, m.p. 152.0-152.8 °C, 101 mg, 96% yield, 93% ee (HPLC: chiralpak AS-H column, 254 nm, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, tr (major) = 14.18 min, tr (minor) = 11.92 min); $[\alpha]_D^{25}$ = +19.1 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.23-7.15 (m, 4H), 7.12-7.03 (m, 6H), 6.95-6.90 (m, 4H), 6.76-6.74 (m, 1H), 4.37-4.26 (m, 2H), 3.81 (s, 3H), 3.73-3.69 (m, 1H), 2.19-2.12 (m, 1H), 2.02-1.95 (m, 1H), 1.38-1.31 (m, 4H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 189.8, 172.1, 171.5, 142.9, 141.3, 135.1, 135.1, 129.3, 128.7, 127.0, 126.9, 126.8, 126.7, 126.7, 124.4, 123.0, 122.9, 58.2, 41.3, 39.7, 35.9, 33.9, 27.1, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2957, 2926, 1751, 1714, 1675, 1595, 1493, 1460, 1408, 1289, 758, 693. HRMS (ESI, *m*/*z*) calcd for $C_{30}H_{30}N_4NaO_3S$ $[M+Na]^+$: 549.1931, found: 549.1931.



3l

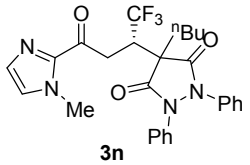
Light yellow oil, 85 mg, 93% yield, 86% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, tr (major) = 21.76 min, tr (minor) = 19.54 min); $[\alpha]_D^{25}$ = +19.0 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.34-7.11 (m, 8H), 7.17-7.12 (m, 3H), 6.99 (s, 1H), 3.93 (s, 3H), 3.45-3.34 (m, 2H), 2.89 (s, 1H), 2.00-1.98 (m, 2H), 1.29 (s, 4H), 1.11 (d, *J* = 3.8 Hz, 3H), 0.84 (t, *J* = 6.4 Hz, 3H), 0.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 191.1, 173.1, 172.8, 143.0, 135.6, 129.2, 129.0, 128.9, 127.0, 126.7, 122.6, 122.6, 56.6, 40.5, 36.1, 35.5, 33.5, 27.1, 22.8, 15.7, 13.7. IR (KBr): *v* (cm^{-1}) 2959, 2927, 1752, 1718, 1673, 1596, 1491, 1460, 1407, 1289, 757, 691. HRMS (ESI, *m*/*z*) calcd for $C_{27}H_{30}N_4NaO_3$ $[M+Na]^+$: 481.2209, found:

481.2210.



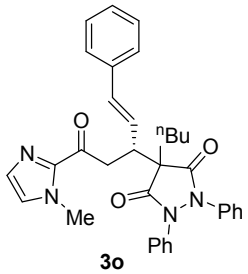
3m

Light yellow oil, 87 mg, 90% yield, 82% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 7.54 min, tr (minor) = 6.34 min); $[\alpha]_D^{25}$ = +61.1 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.29 (m, 8H), 7.15 (s, 3H), 7.02 (m, 1H), 3.95 (m, 4H), 3.27-3.21 (m, 1H), 3.02 (s, 1H), 2.04-1.85 (m, 3H), 1.26-1.13 (m, 4H), 0.96-0.75 (m, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 192.0, 173.5, 173.2, 142.9, 135.7, 129.2, 129.0, 128.8, 127.0, 126.6, 126.6, 126.4, 122.5, 122.4, 122.2, 56.0, 44.8, 36.1, 35.9, 33.2, 29.3, 26.8, 23.1, 22.7, 17.4, 13.6. IR (KBr): *v* (cm^{-1}) 2959, 2928, 2872, 1718, 1675, 1596, 1493, 1460, 1407, 1286, 757, 691. HRMS (ESI, *m*/*z*) calcd for $C_{29}H_{34}N_4NaO_3$ $[M+Na]^+$: 509.2522, found: 509.2523.



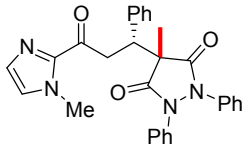
3n

White solid, m.p. 154.1-154.4 °C, 109 mg, 95% yield, 97% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 15.59 min, tr (minor) = 13.52 min); $[\alpha]_D^{25}$ = +17.8 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.47-7.45 (m, 3H), 7.30-7.25 (m, 11H), 7.21 (s, 1H), 7.18-7.15 (m, 2H), 4.20-4.14 (m, 1H), 3.89-3.83 (m, 1H), 3.71-3.65 (m, 1H), 1.89-1.85 (m, 2H), 1.30-1.23 (m, 4H), 0.79 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.6, 170.7, 170.2, 142.0, 138.1, 135.3, 135.2, 130.3, 129.1, 129.0, 128.99, 128.98, 127.7, 127.03, 127.0, 125.9, 122.9, 122.8, 50.7, 43.0 (q, *J* = 25.9 Hz), 34.9, 33.7, 25.9, 22.6, 13.6. ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -66.2. IR (KBr): *v* (cm^{-1}) 2959, 2926, 1758, 1721, 1691, 1596, 1493, 1459, 1303, 1121, 759, 691. HRMS (ESI, *m*/*z*) calcd for $C_{32}H_{29}F_3N_4NaO_3$ $[M+Na]^+$: 597.2082, found: 597.2084.



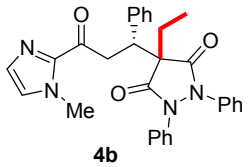
3o

Colourless oil, 104 mg, 95% yield, 93% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, tr (major) = 20.74 min, tr (minor) = 16.70 min); $[\alpha]_D^{25}$ = +16.0 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.26-7.09 (m, 16H), 6.95 (s, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 6.19-6.13 (m, 1H), 3.86-3.78 (m, 4H), 3.61-3.56 (m, 1H), 3.29 (d, *J* = 15.0 Hz, 1H) 2.02-2.00 (m, 2H), 1.30-1.26 (m, 4H), 0.85 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.2, 172.5, 172.4, 143.4,143.1, 141.7, 136.6, 135.5, 135.4, 134.3, 129.2,128.9, 128.8, 128.4, 128.4, 127.6, 127.3, 127.3, 127.2, 127.0, 126.7, 126.7, 126.6, 126.5, 126.5, 122.8, 122.7, 56.8, 44.9,38.7, 36.0, 33.9, 27.1, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2924, 2855, 1752, 1717, 1675, 1595, 1493, 1460, 1407, 1290, 754, 692. HRMS (ESI, *m*/*z*) calcd for $C_{34}H_{34}N_4NaO_3$ $[M+Na]^+$: 569.2522, found: 569.2523.



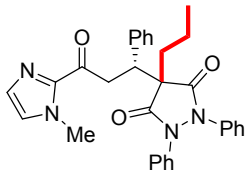
4a

Light yellow oil, 92 mg, 96% yield, 94% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 19.99 min, tr (minor) = 14.78 min); $[\alpha]_D^{25}$ = +13.6 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.28 (m, 2H), 7.20-7.02 (m, 10H), 6.94 (d, *J* = 8.0 Hz, 3H), 6.73 (d, *J* = 7.5 Hz, 2H), 4.40-4.33 (m, 1H), 4.06-4.03 (m, 1H), 3.79 (s, 3H), 3.78-3.70 (m, 1H), 1.64 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.5, 172.7, 171.8, 143.0, 138.5, 135.1, 135.0, 129.2, 129.1, 129.0, 128.6, 128.5, 127.5, 126.9, 126.8, 126.7, 123.0, 122.9, 122.5, 52.6, 46.3, 37.8, 35.9, 19.4. IR (KBr): *v* (cm^{-1}) 2920, 2851, 1750, 1713, 1675, 1596, 1493, 1456, 1407, 1384, 756, 734, 691. HRMS (ESI, *m*/*z*) calcd for $C_{29}H_{26}N_4NaO_3$ $[M+Na]^+$: 501.1896, found: 501.1897.



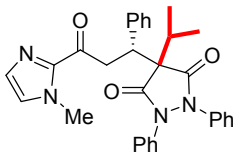
4b

Light yellow oil, 88 mg, 90% yield, 95% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 21.51 min, tr (minor) = 17.31 min); $[\alpha]_D^{25}$ = +18.0 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.31-7.29 (m, 2H), 7.20-7.02 (m, 10H), 6.94 (t, *J* = 7.8 Hz, 3H), 6.75 (d, *J* = 7.6 Hz, 2H), 4.33-4.26 (m, 1H), 4.08-4.04 (m, 1H), 3.80-3.75 (m, 1H), 3.77 (s, 3H), 2.27-2.17 (m, 1H), 2.07-2.01 (m, 1H), 0.98 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.5, 172.1, 171.6, 143.0, 138.6, 135.0, 134.9, 129.2, 129.2, 128.6, 128.6, 128.4, 127.4, 126.9, 126.7, 126.7, 123.0, 122.9, 58.8, 45.9, 38.1, 35.9, 27.3, 9.6. IR (KBr): *v* (cm^{-1}) 2968, 2924, 1750, 1713, 1675, 1595, 1494, 1457, 1408, 1289, 756, 696. HRMS (ESI, *m/z*) calcd for $C_{30}H_{28}N_4NaO_3$ $[M+Na]^+$: 515.2054, found: 515.2054.



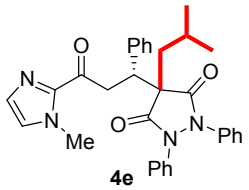
4c

Light yellow oil, 96 mg, 95% yield, >99% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 34.48 min, tr (minor) = 27.71 min); $[\alpha]_D^{25}$ = +20.8 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.26 (m, 2H), 7.20-7.02 (m, 10H), 6.93 (d, *J* = 8.2 Hz, 3H), 6.73 (d, *J* = 7.6 Hz, 2H), 4.40-4.33 (m, 1H), 4.07-4.03 (m, 1H), 3.77 (s, 3H), 3.76-3.71 (m, 1H), 2.19-2.12 (m, 1H), 2.01-1.94 (m, 1H), 1.42-1.32 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.5, 172.2, 171.7, 143.0, 138.5, 135.0, 134.9, 129.2, 129.2, 128.6, 128.6, 128.4, 127.4, 126.9, 126.7, 126.6, 123.0, 122.9, 58.1, 46.2, 38.0, 36.2, 35.9, 18.6, 14.2. IR (KBr): *v* (cm^{-1}) 2961, 2926, 1752, 1713, 1675, 1595, 1494, 1457, 1407, 1283, 758, 694. HRMS (ESI, *m/z*) calcd for $C_{31}H_{30}N_4NaO_3$ $[M+Na]^+$: 529.2208, found: 529.2210.



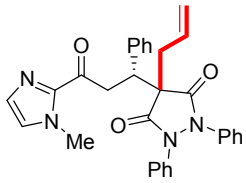
4d

Light yellow oil, 93 mg, 92% yield, >99% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 39.43 min, tr (minor) = 20.82 min); $[\alpha]_D^{25}$ = +12.7 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.31-7.28 (m, 2H), 7.18 (t, *J* = 7.6 Hz, 2H), 7.12-7.01 (m, 8H), 6.94 (t, *J* = 7.6 Hz, 3H), 6.64 (d, *J* = 7.72 Hz, 2H), 4.62-4.54 (m, 1H), 4.20-4.16 (m, 1H), 3.75 (s, 3H), 3.54-3.49 (m, 1H), 1.40 (d, *J* = 6.9 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.6, 172.0, 171.3, 143.1, 138.2, 135.1, 134.9, 129.5, 129.2, 128.6, 128.5, 128.4, 127.3, 126.8, 126.6, 126.5, 123.1, 122.8, 60.4, 43.4, 37.1, 35.9, 32.0, 32.0, 18.9, 15.6. IR (KBr): *v* (cm^{-1}) 2964, 2926, 1747, 1711, 1674, 1595, 1494, 1459, 1406, 1289, 739, 691. HRMS (ESI, *m*/*z*) calcd for $C_{31}H_{30}N_4NaO_3$ $[M+Na]^+$: 529.2205, found: 529.2210.



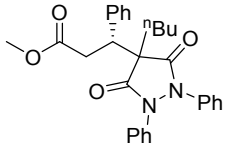
4e

Light yellow oil, 97 mg, 93% yield, 85% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol =80/20, flow rate 1.0 mL/min, tr (major) = 34.73 min, tr (minor) = 26.01 min); $[\alpha]_D^{25}$ = +17.1 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.26 (m, 2H), 7.19-7.02 (m, 10H), 6.90 (d, *J* = 8.0 Hz, 3H), 6.67 (d, *J* = 7.7 Hz, 2H), 4.42-4.34 (m, 1H), 4.02-3.99 (m, 1H), 3.98 (s, 3H), 3.74-3.68 (m, 1H), 2.18-2.13 (m, 1H), 2.03-1.99 (m, 1H), 1.81-1.75 (m, 1H), 0.95-0.88 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.4, 171.8, 171.3, 143.0, 138.1, 134.8, 134.8, 129.3, 129.1, 128.6, 128.5, 128.4, 127.4, 126.8, 126.6, 126.5, 122.9, 122.7, 47.9, 42.7, 38.0, 35.9, 25.9, 24.1, 22.8. IR (KBr): *v* (cm^{-1}) 2959, 2872, 1752, 1714, 1677, 1596, 1494, 1457, 1408, 1288, 757, 700. HRMS (ESI, *m*/*z*) calcd for $C_{32}H_{32}N_4NaO_3$ $[M+Na]^+$: 543.2366, found: 543.2367.



4f

Light yellow oil, 95 mg, 94% yield, 97% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 60/40, flow rate 1.0 mL/min, tr (major) = 41.95 min, tr (minor) = 23.57 min); $[\alpha]_D^{25}$ = +13.2 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.29 (m, 2H), 7.19-7.02 (m, 10H), 6.92 (t, *J* = 7.8 Hz, 3H), 6.72 (d, *J* = 7.7 Hz, 2H), 5.80-5.69 (m, 1H), 5.25-5.11 (m, 2H), 4.37-4.30 (m, 1H), 4.11-4.07 (m, 1H), 3.81-3.76 (m, 1H), 3.79 (s, 3H), 2.93-2.71 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.3, 171.4, 170.9, 142.9, 138.4, 134.9, 134.8, 130.9, 129.3, 129.2, 128.6, 128.6, 128.5, 127.4, 126.9, 126.8, 126.7, 123.3, 123.2, 121.0, 58.1, 45.6, 38.0, 37.9, 35.9. IR (KBr): *v* (cm^{-1}) 3064, 2922, 1749, 1713, 1676, 1597, 1494, 1456, 1408, 1284, 758, 701. HRMS (ESI, *m*/*z*) calcd for $C_{31}H_{28}N_4NaO_3$ $[M+Na]^+$: 527.2057, found: 527.2059.



5

Light yellow oil, DBU as the base: 81 mg, 89% yield, 97% ee; CH_3ONa as the base: 83 mg, 91% yield, 97% ee; (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, tr (major) = 7.88 min, tr (minor) = 16.27 min); $[\alpha]_D^{25}$ = -13.6 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.25 (m, 1H), 7.24-7.16 (m, 6H), 7.14-7.04 (m, 4H), 6.91 (t, *J* = 9.9 Hz, 2H), 6.70 (t, *J* = 7.4 Hz, 2H), 3.82-3.78 (m, 1H), 3.50 (s, 3H), 3.32-3.25 (m, 1H), 3.17-3.12 (m, 1H), 2.13-1.94 (m, 2H), 1.35-1.29 (m, 4H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.1, 171.8, 171.5, 137.9, 134.8, 134.7, 129.0, 128.7, 128.6, 127.7, 126.9, 123.1, 123.1, 122.6, 57.7, 51.7, 46.9, 33.7, 33.6, 27.1, 22.8, 13.7. IR (KBr): *v* (cm^{-1}) 2957, 2924, 1746, 1717,1630, 1595, 1494, 1457, 1298, 757, 700. HRMS (ESI, *m*/*z*) calcd for $C_{29}H_{30}N_2NaO_4$ $[M+Na]^+$: 493.2094, found: 493.2098.

IV. Single Crystal X-Ray Diffraction of 3n

Single-crystal data of **3n** were collected at 293 K with SuperNova diffractometer which is equipped with a copper micro-focus X-ray sources (λ = 1.54184 Å). The structure was solved by direct methods and refined on F^2 by full-matrix least squares using the *SHELXL*-2017 crystallographic software package.[5] Hydrogen atoms were generated theoretically onto the specific atoms and refined isotropically with fixed thermal factors. The crystal data and structure refinement of **3n** are summarized in Table 1. CCDC 1832329 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from Cambridge Crystallographic Data Centre *via* www.ccdc. cam.ac.uk/conts/retrieving.html.

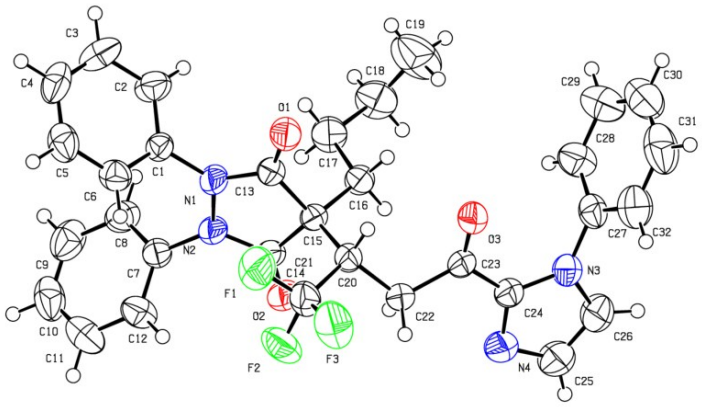


Figure S1. The structure of **3n**. Displacement ellipsoids are plotted at the 50% probability level.

Table 1. Crystal data and structure refinement for 3n.

Identification code	compound-**3n**	
Empirical formula	$C_{32}H_{29}F_3N_4O_3$	
Formula weight	574.59	
Temperature (K)	293(2)	
Wavelength (Å)	1.54184	
Crystal system	monoclinic	
Space group	$P2_1$	
Unit cell dimensions (Å, °)	a = 10.5588(2)	α = 90
	b = 11.2682(2)	β = 90.698(2)
	c = 12.1940(2)	γ = 90
Volume (Å)	1450.72(4)	
Z	2	
Calculated density (g cm^{-3})	1.315	
Absorption coefficient (mm^{-1})	0.826	
F_{000}	600	
Crystal size (mm^3)	0.150 × 0.120 × 0.120	

θ range for data collection (°)	3.625 to 73.420
Miller index ranges	$-13 \le h \le 12$, $-13 \le k \le 11$, $-10 \le l \le 15$
Reflections collected	9813
Independent reflections	4897 [$R_{int} = 0.0183$]
Completeness to θ_{max} (%)	0.985
Max. and min. transmission	0.80789 and 1.00000
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4897 / 8 / 381
Goodness-of-fit on F^2	0.927
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0295$, $wR2 = 0.0792$
R indices (all data)	$R1 = 0.0311$, $wR2 = 0.0812$
Extinction coefficient	0.0383(12)
Largest diff. peak and hole (e Å^{-3})	0.125 and -0.107
Absolute structure parameter	.02(8)

V References

(1) (a) Wang, C.; Chen, L.-A.; Huo, H.; Shen, X.; Harms, K.; Gong, L.; Meggers, E. *Chem. Sci.* **2015**, *6*, 1094-1100. (b) Sun, G.-J.; Gong, J.; Kang, Q. *J. Org. Chem.* **2017**, *82*, 796. (c) Li, S.-W.; Gong, J.; Kang, Q. *Org. Lett*. **2017**, *19*, 1350. (d) Li, K.; Wan, Q.; Kang, Q. *Org. Lett*. **2017**, *19*, 3299. (e) Lin, S.-X.; Sun, G.-J.; Kang, Q. *Chem. Commun.* **2017**, *53*, 7665.

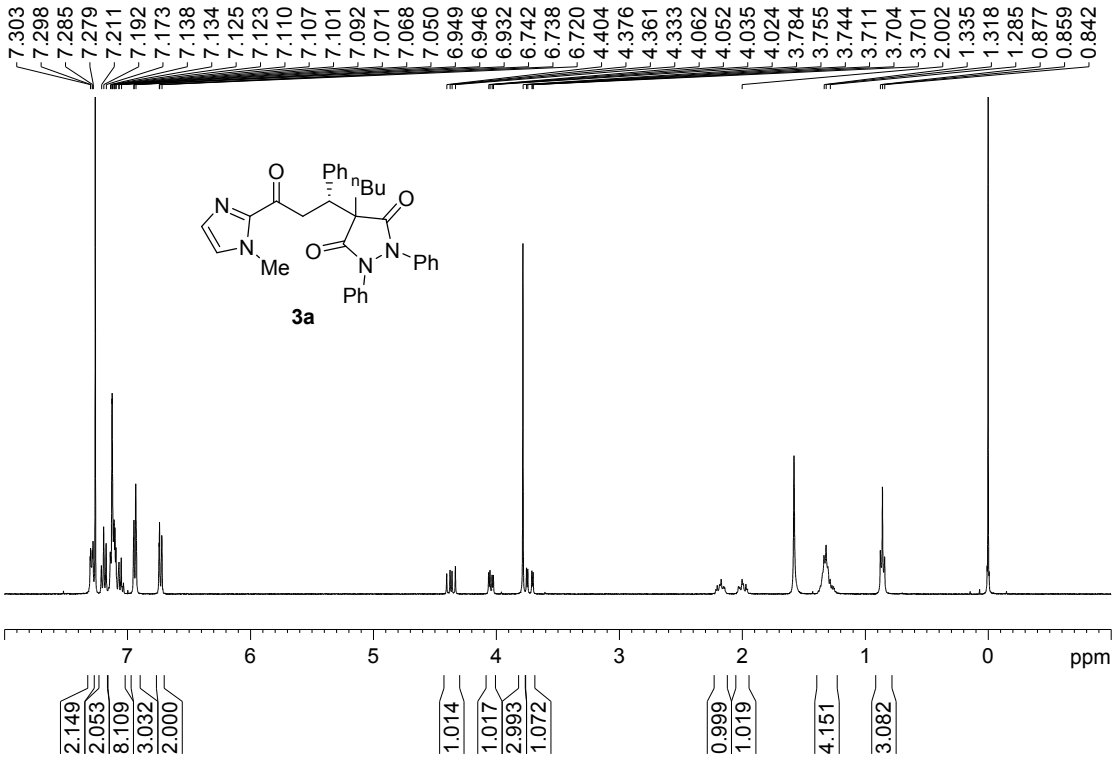
(2) Huo, H.; Fu, C.; Harms, K.; Meggers, E. *J. Am. Chem. Soc*. **2014**, *136*, 2990-2993.

(3) Geigy, A.G. U.S. Patent 2562830, 1949.

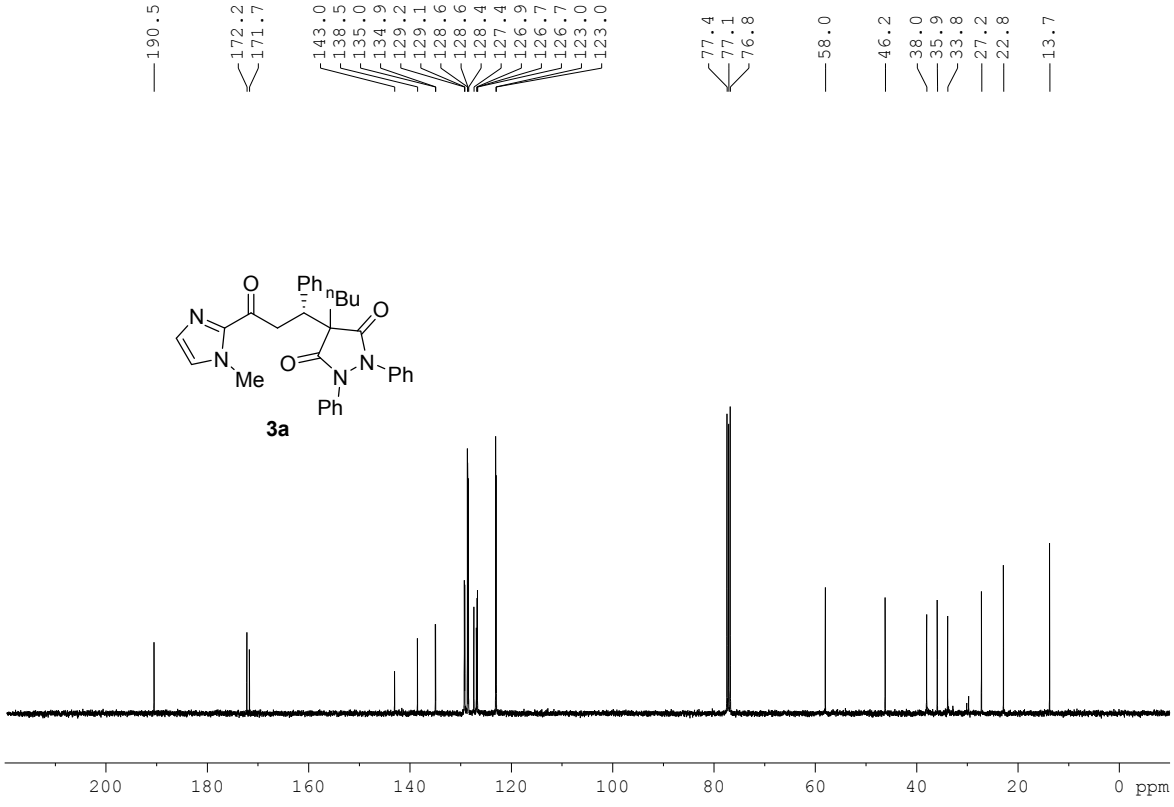
(4) Locock, R.A.; Moskalyk, R.E.; Chatten, L.G. *J. Pharm. Sci.* **1974**, *63*, 1896-1901.

(5) G. M. Sheldrick, *Acta Crystlogr. C Struct. Chem.*, 2015, C**71**, 3-8.

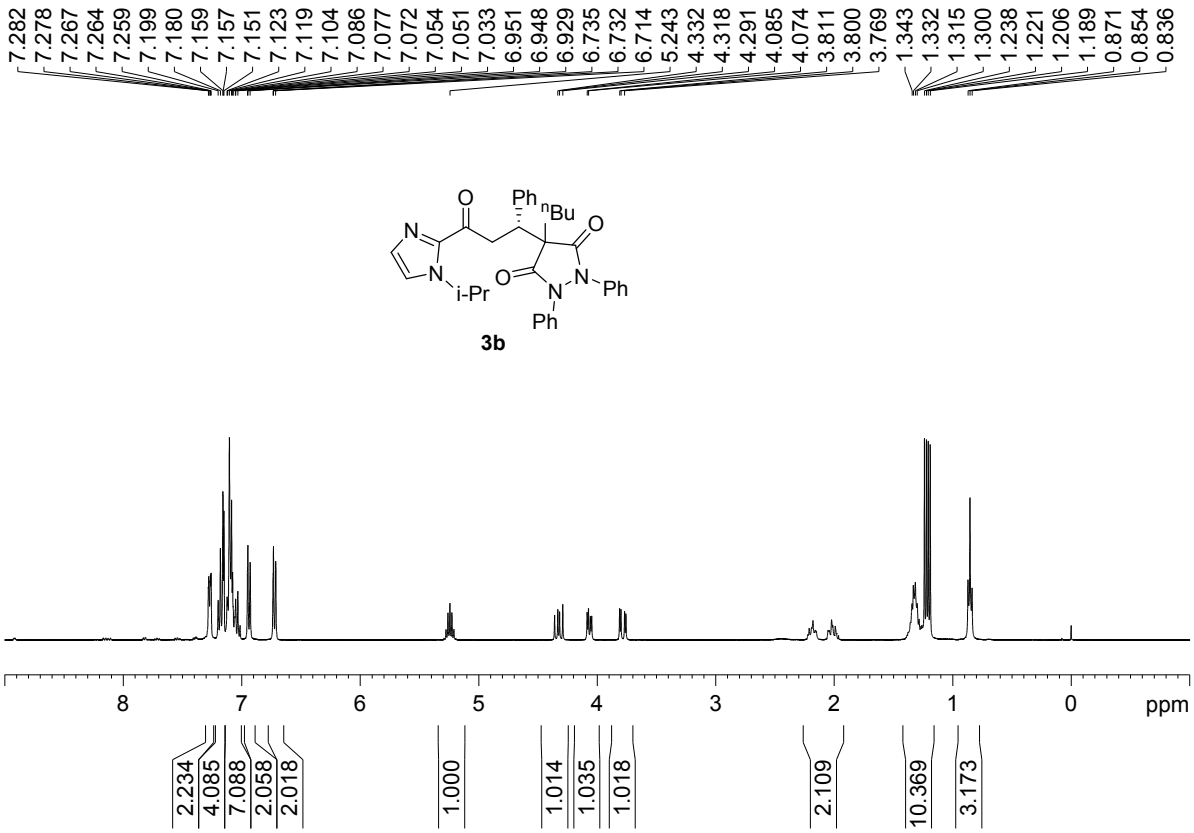
VI NMR Spectrum



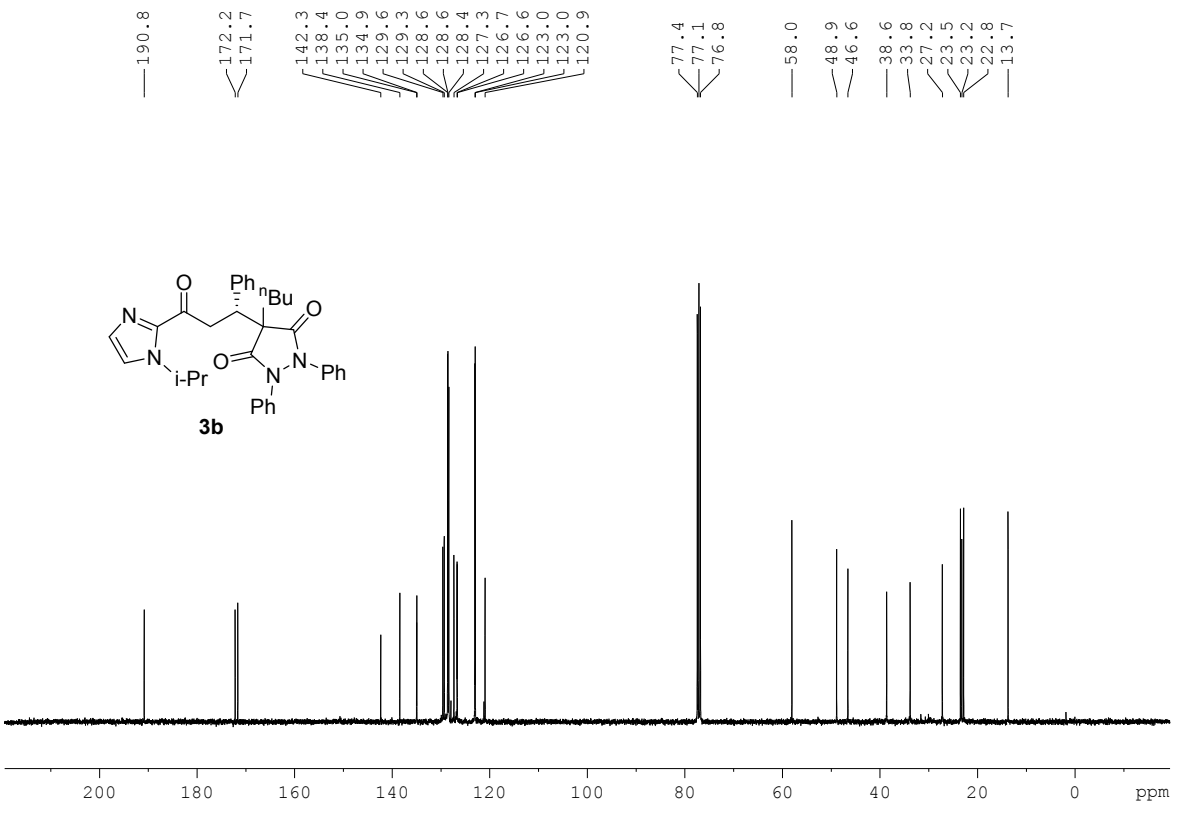
^{1}H NMR (400 MHz) spectra of **3a**



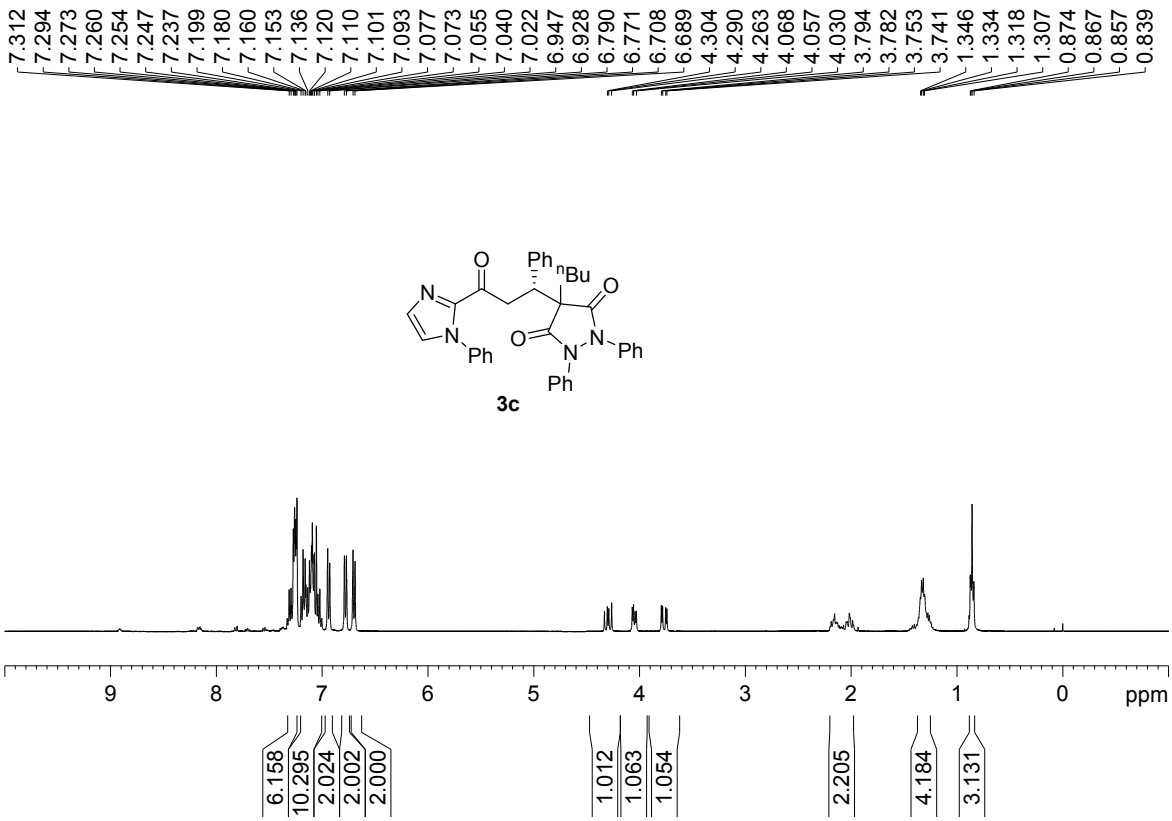
^{13}C NMR (100 MHz) spectra of **3a**



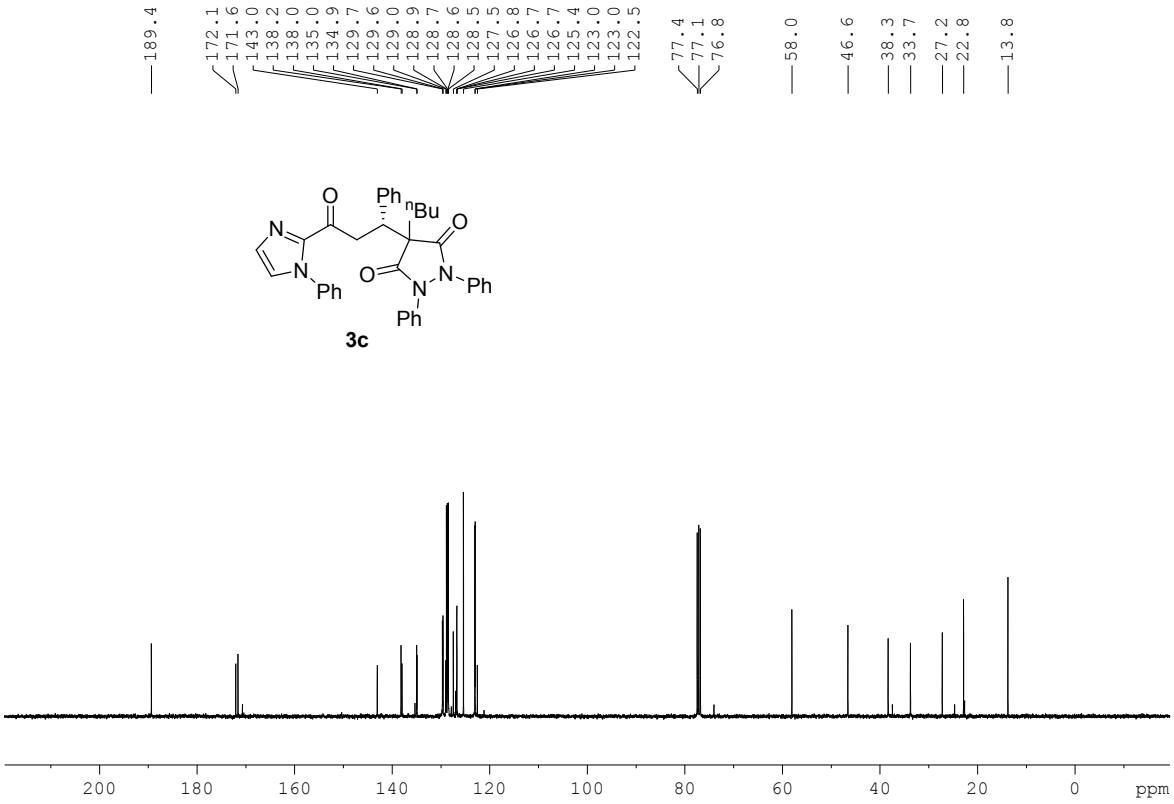
^{1}H NMR (400 MHz) spectra of **3b**



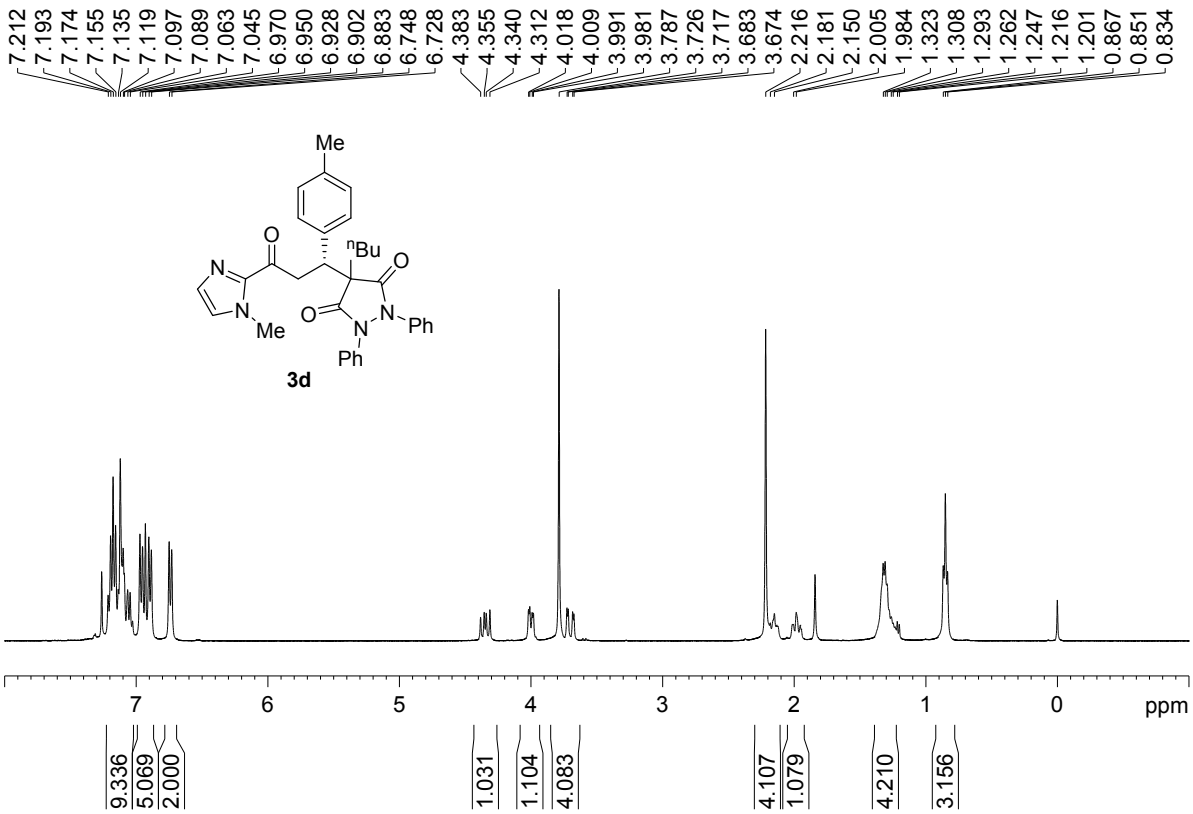
^{13}C NMR (100 MHz) spectra of **3b**



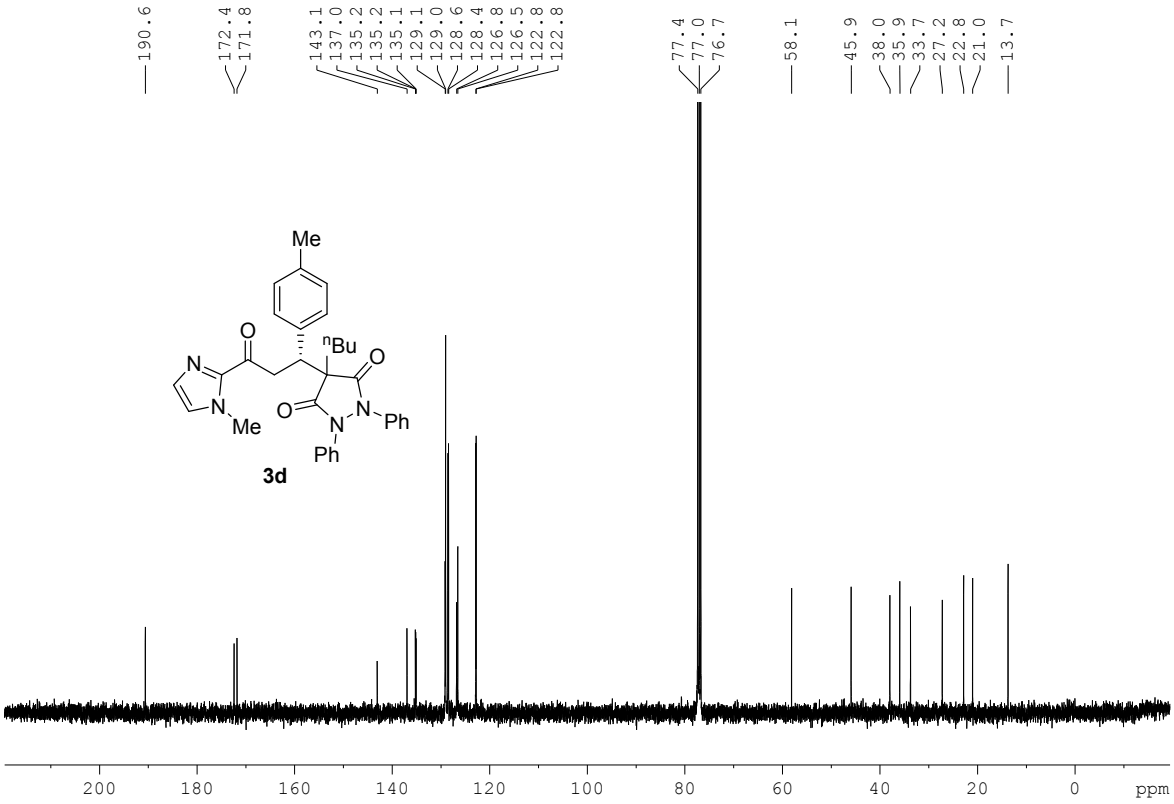
^{1}H NMR (400 MHz) spectra of **3c**



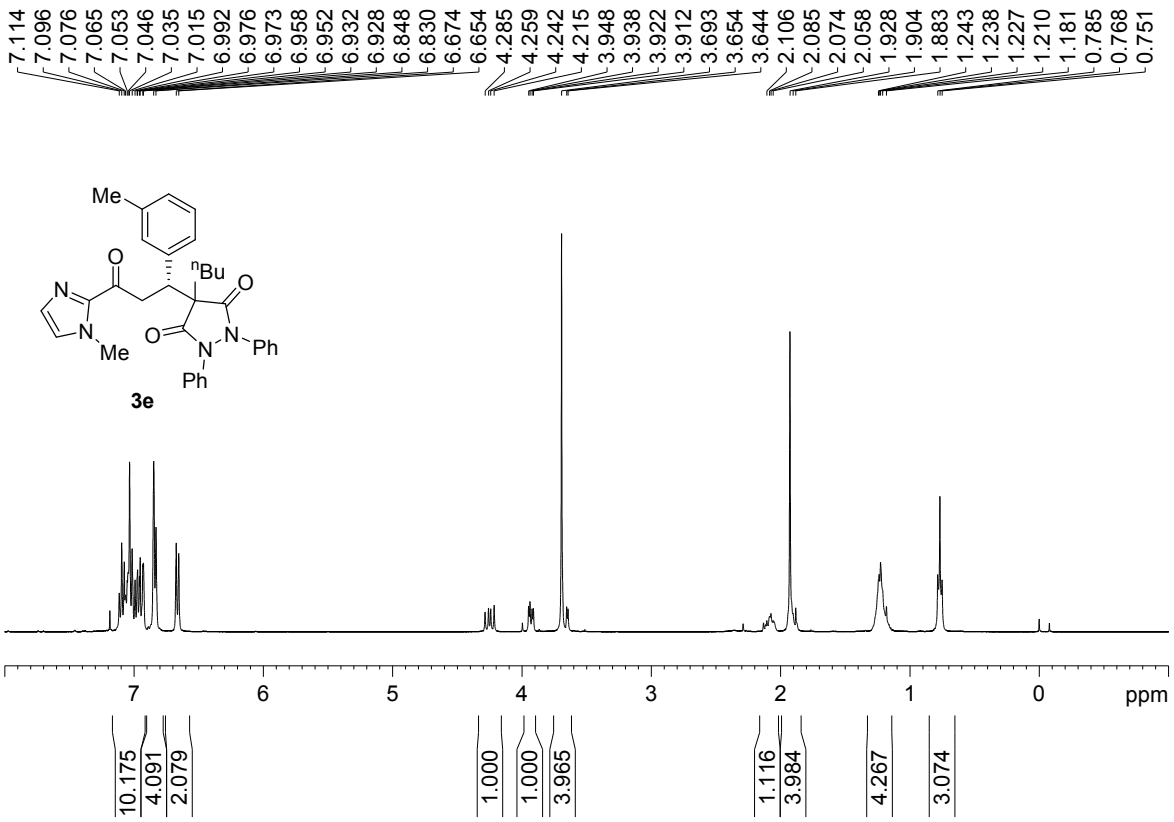
^{13}C NMR (100 MHz) spectra of **3c**



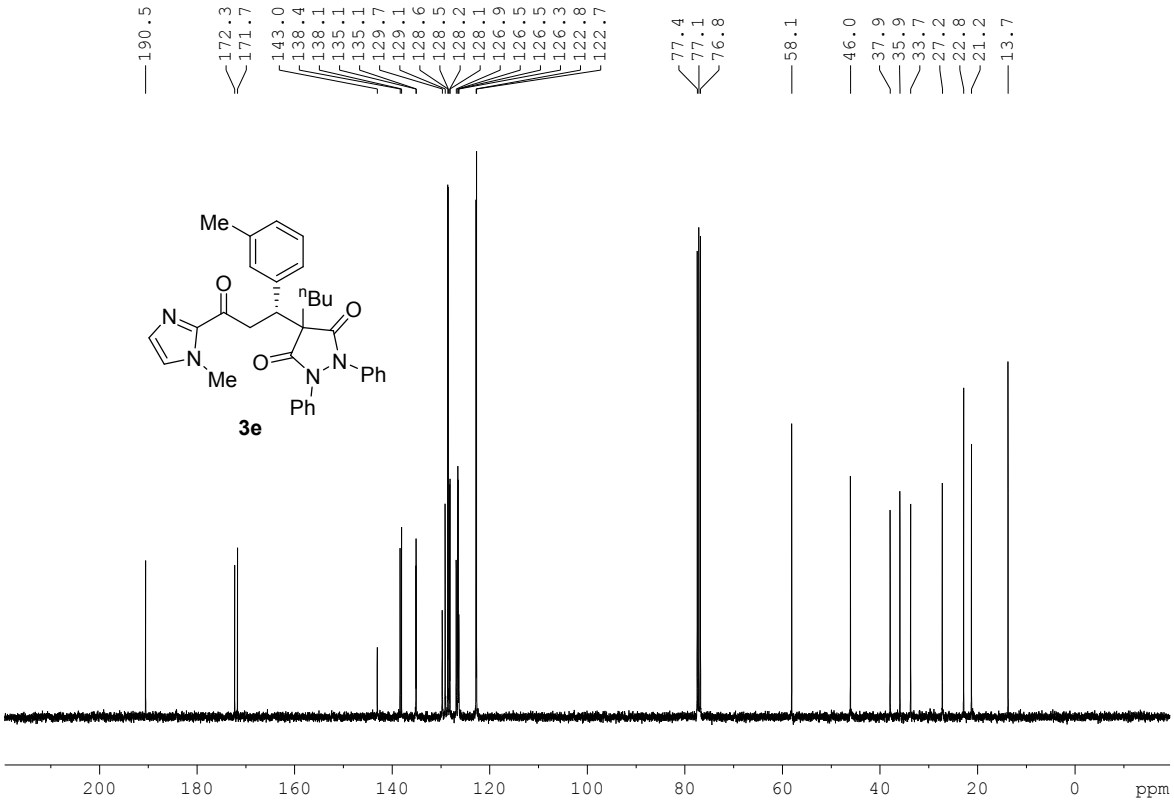
^{1}H NMR (400 MHz) spectra of **3d**



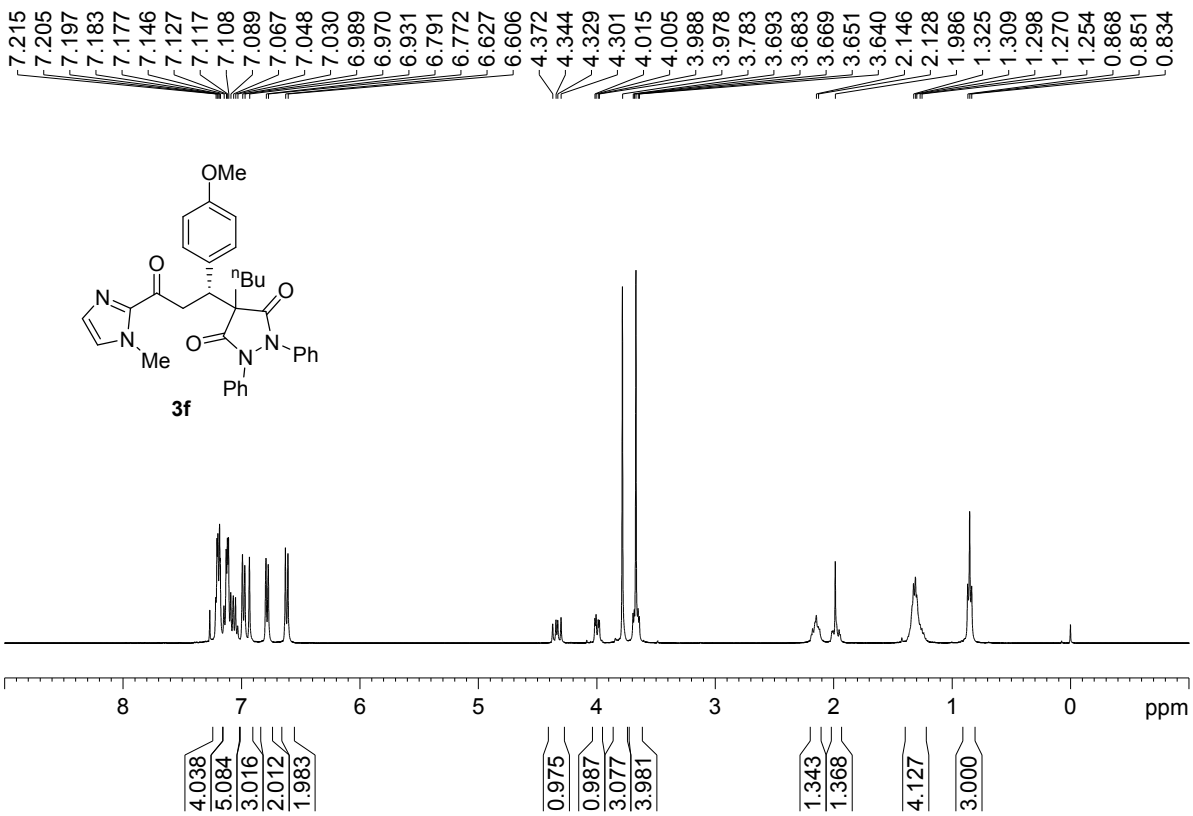
^{13}C NMR (100 MHz) spectra of **3d**



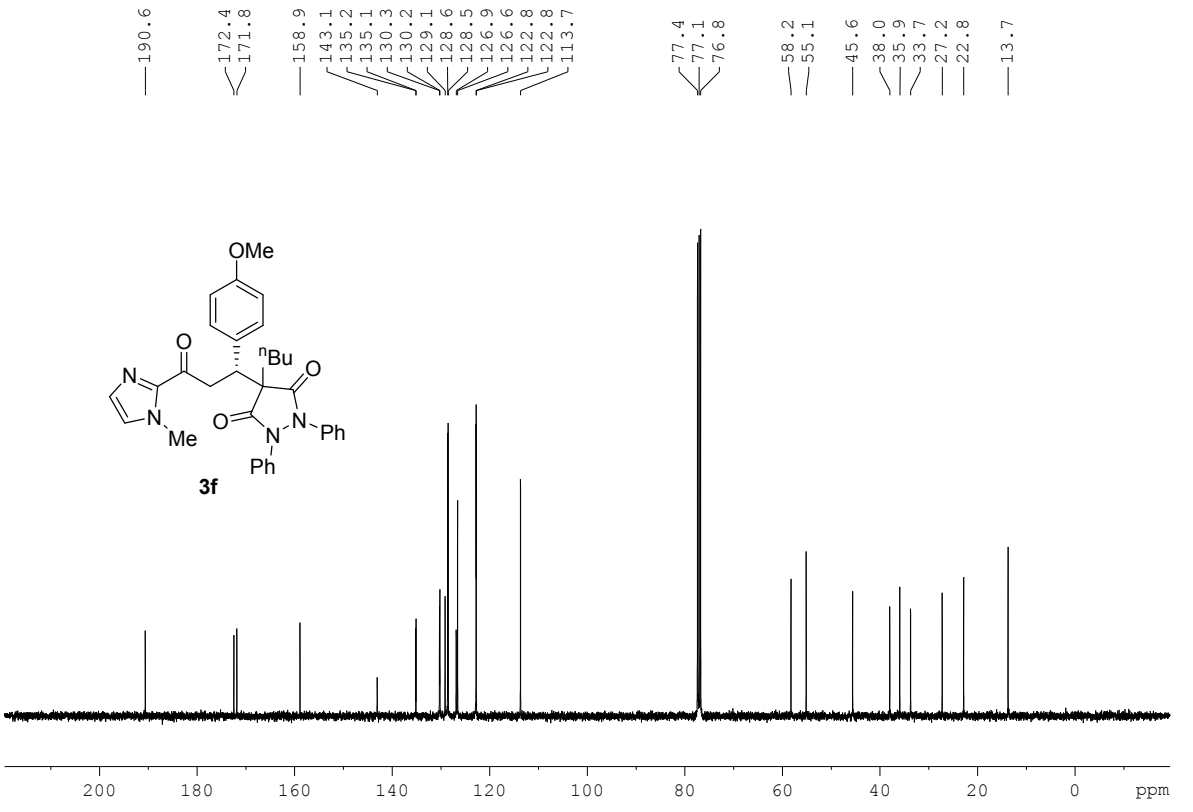
^{1}H NMR (400 MHz) spectra of **3e**



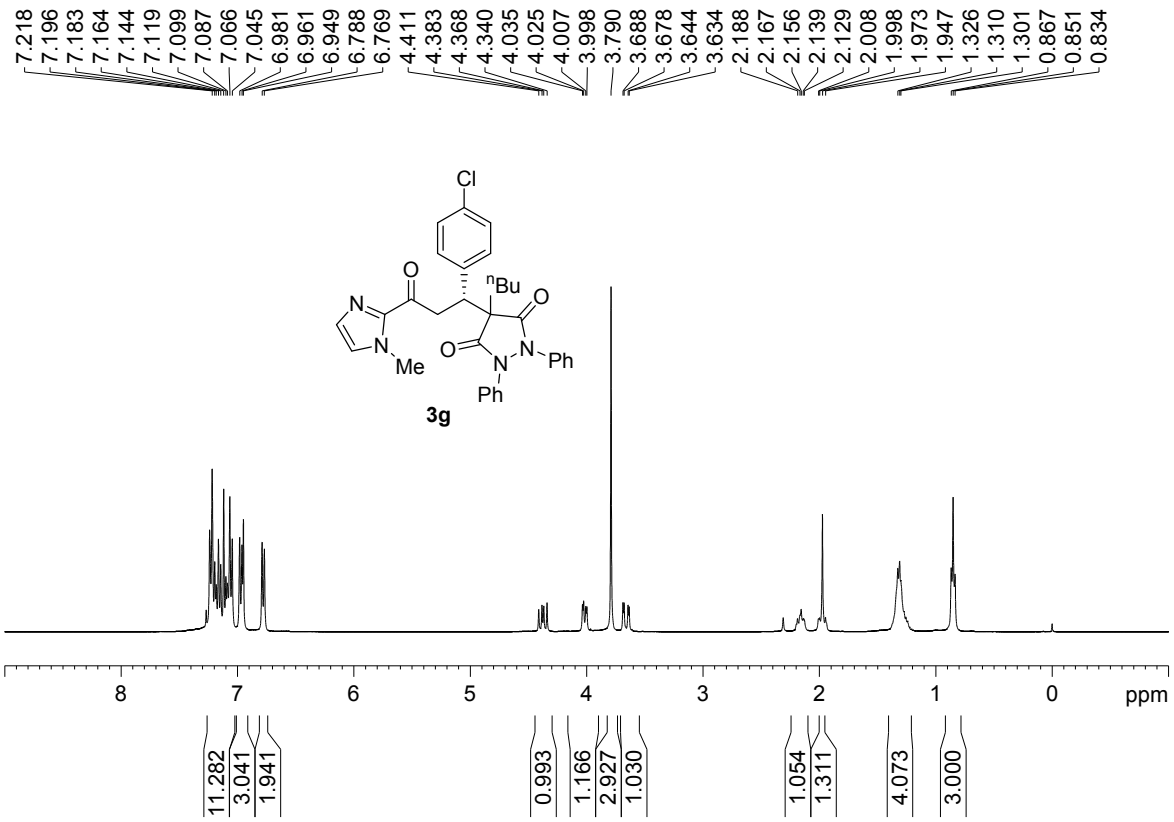
^{13}C NMR (100 MHz) spectra of **3e**



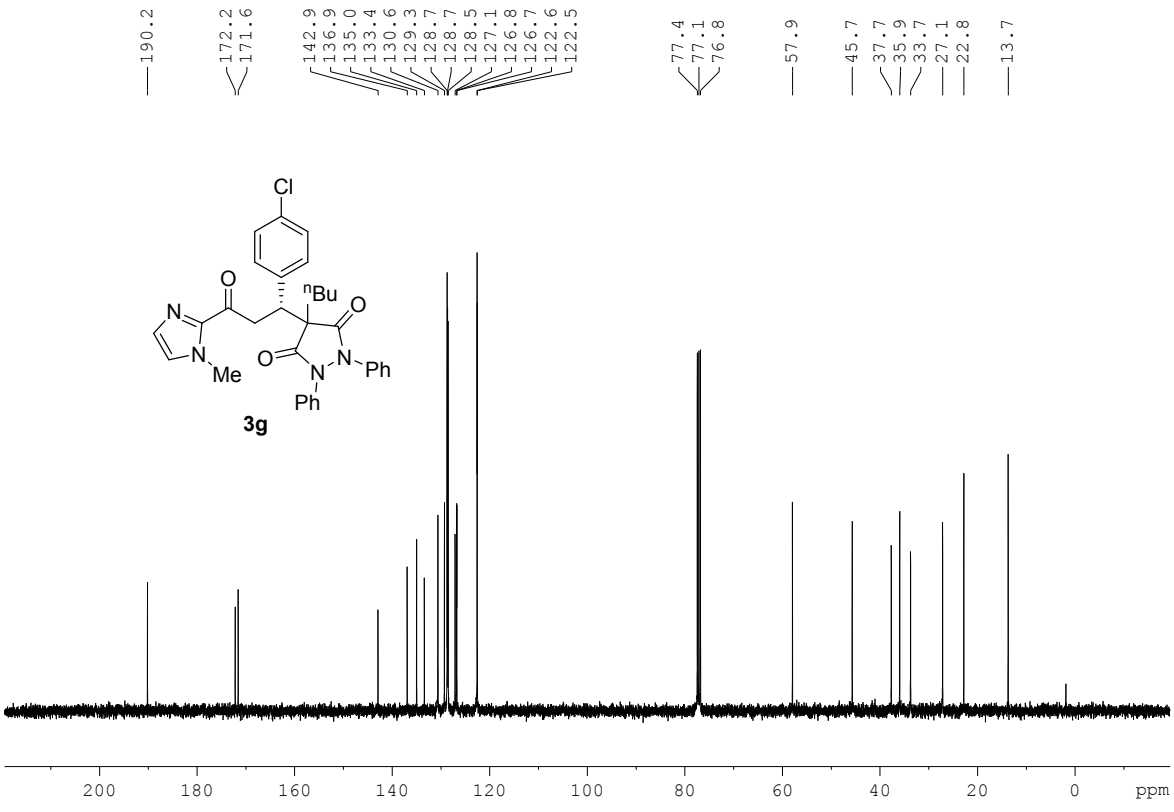
^{1}H NMR (400 MHz) spectra of **3f**



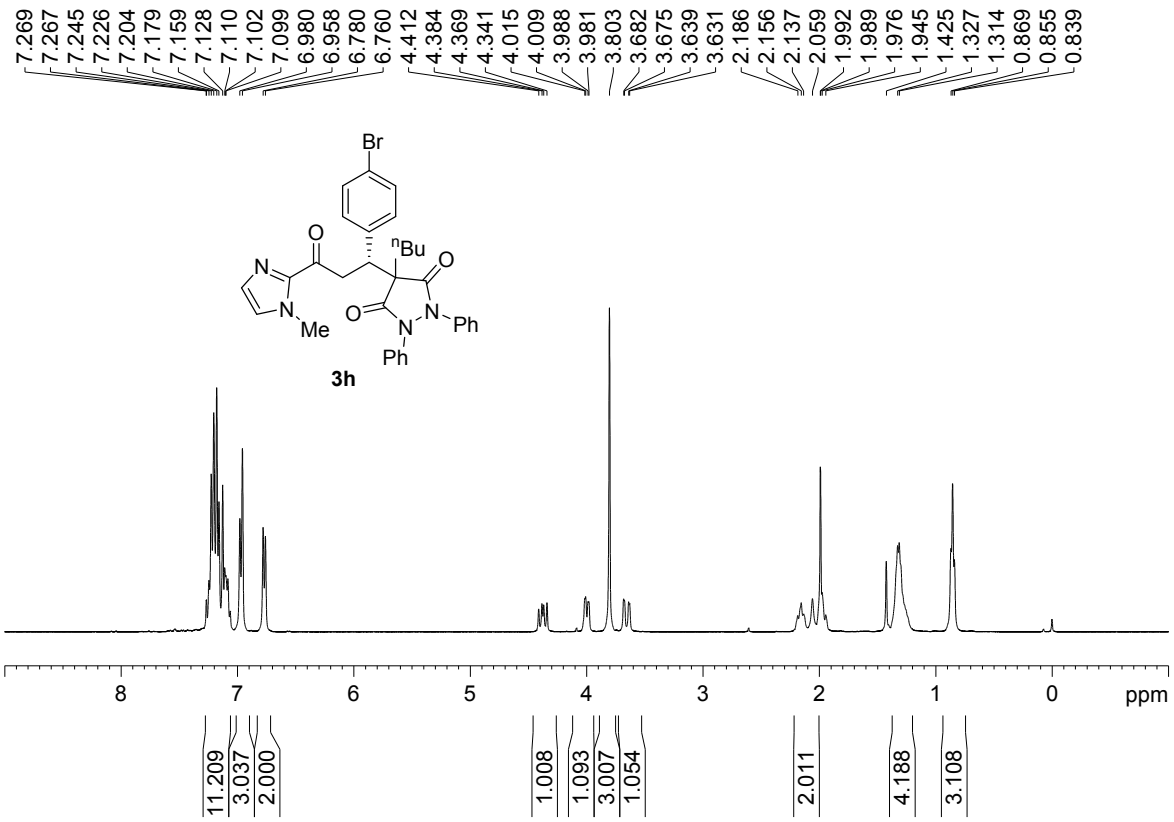
^{13}C NMR (100 MHz) spectra of **3f**



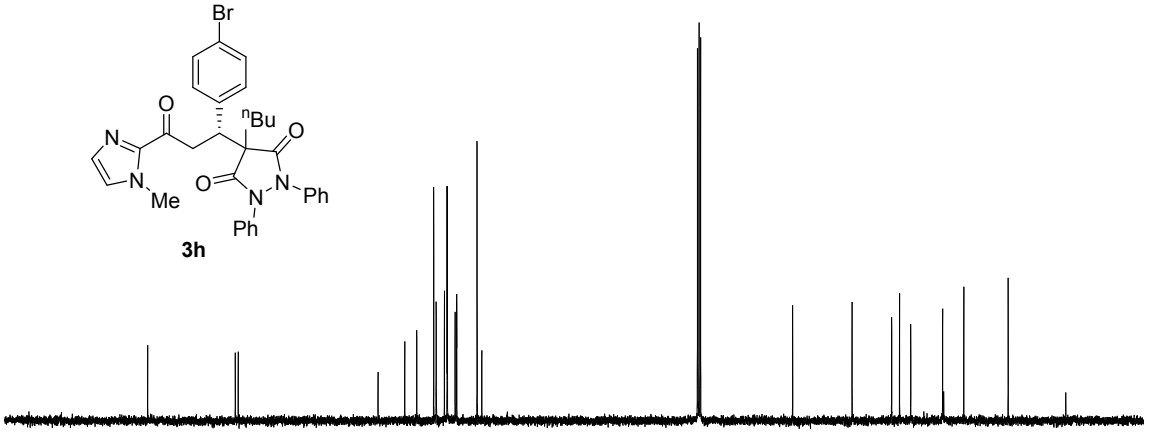
^{1}H NMR (400 MHz) spectra of **3g**



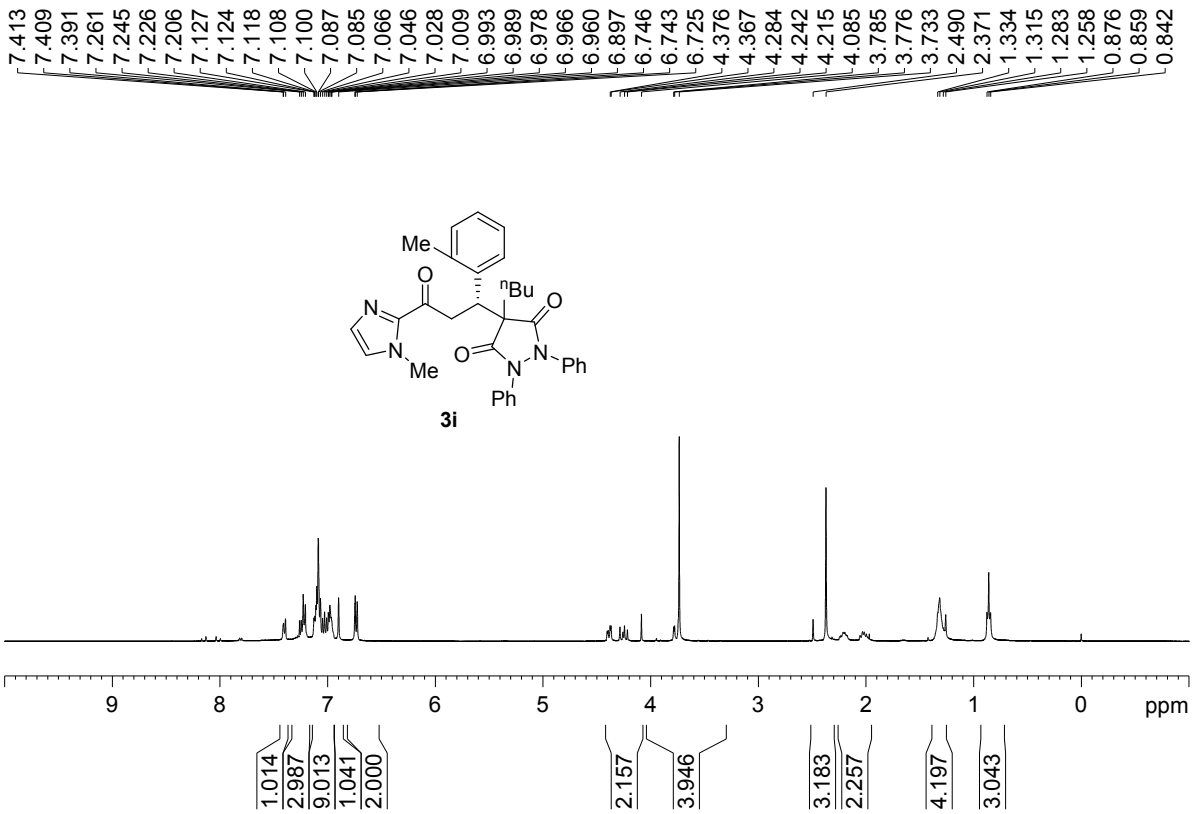
^{13}C NMR (100 MHz) spectra of **3g**



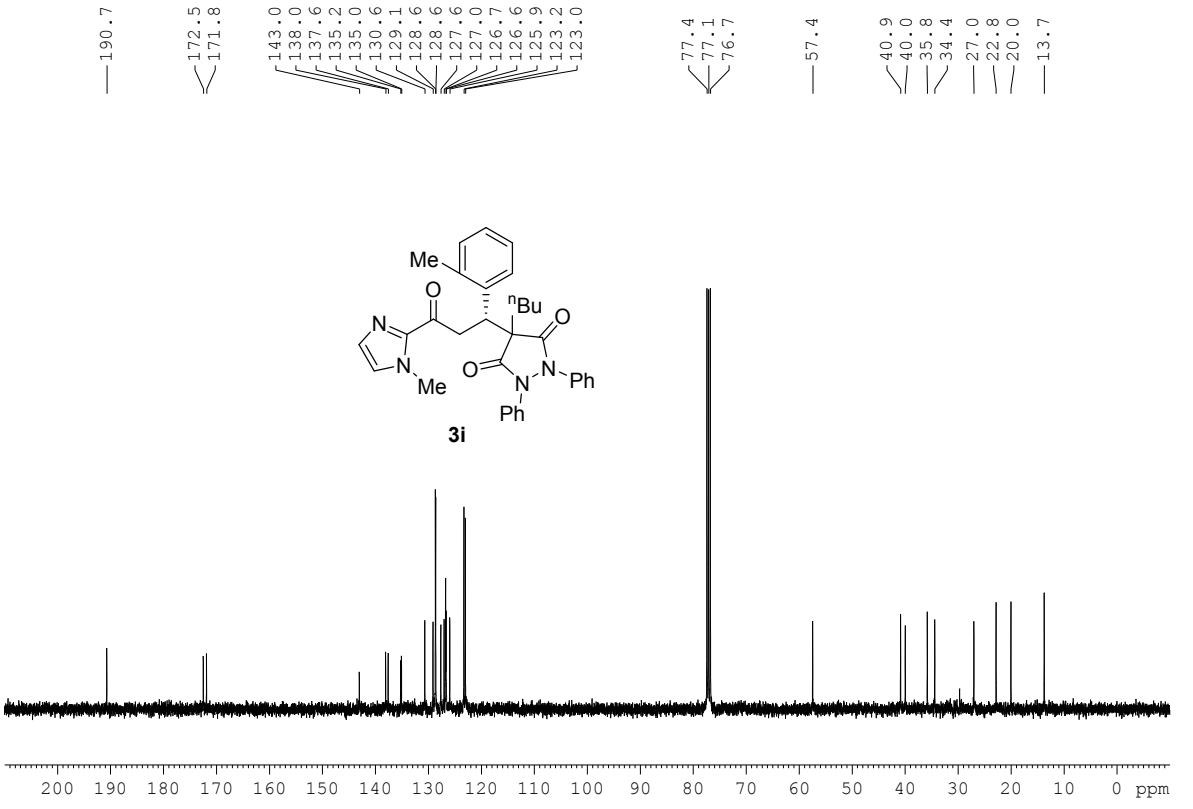
^{1}H NMR (400 MHz) spectra of **3h**



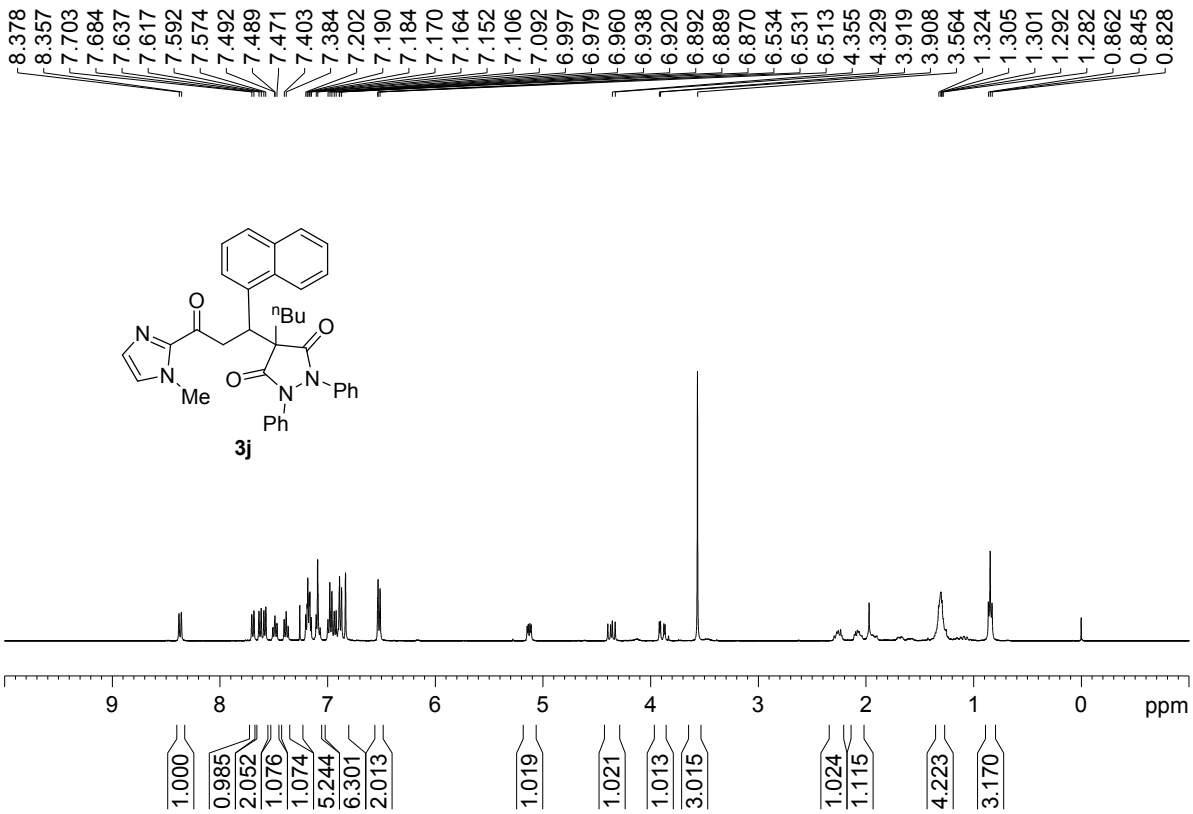
^{13}C NMR (100 MHz) spectra of **3h**



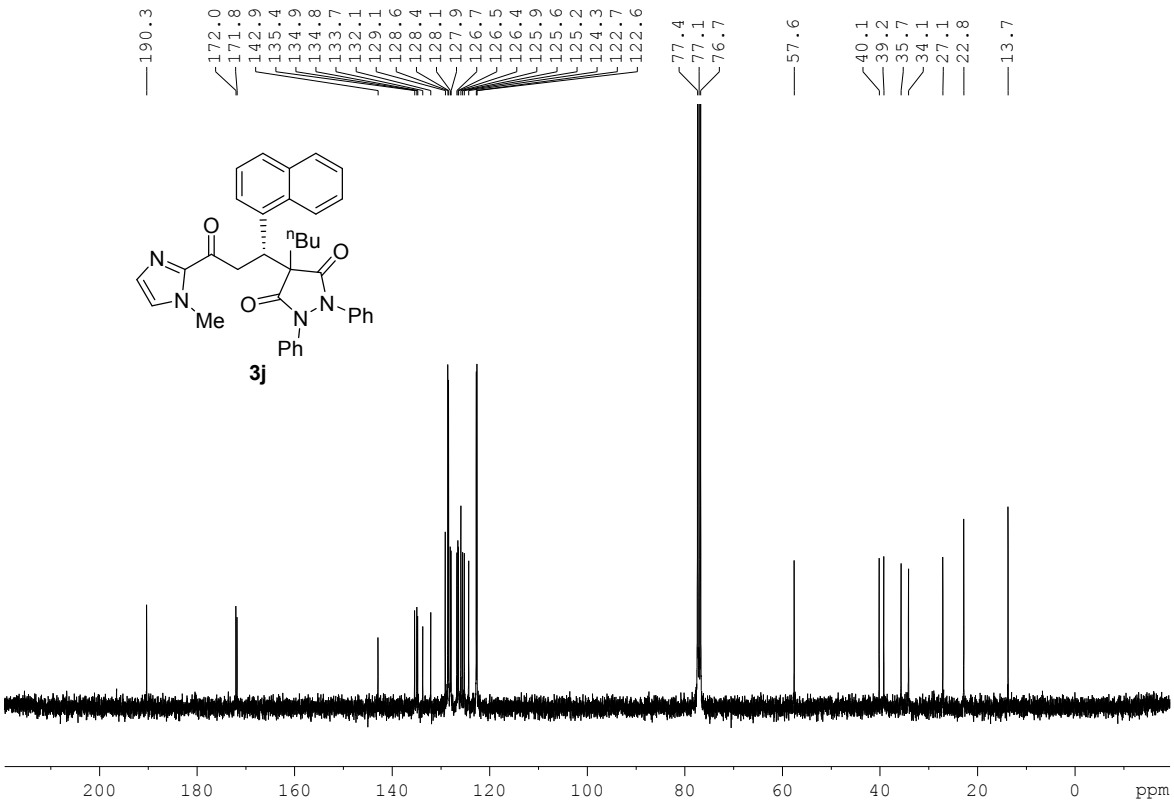
^{1}H NMR (400 MHz) spectra of **3i**



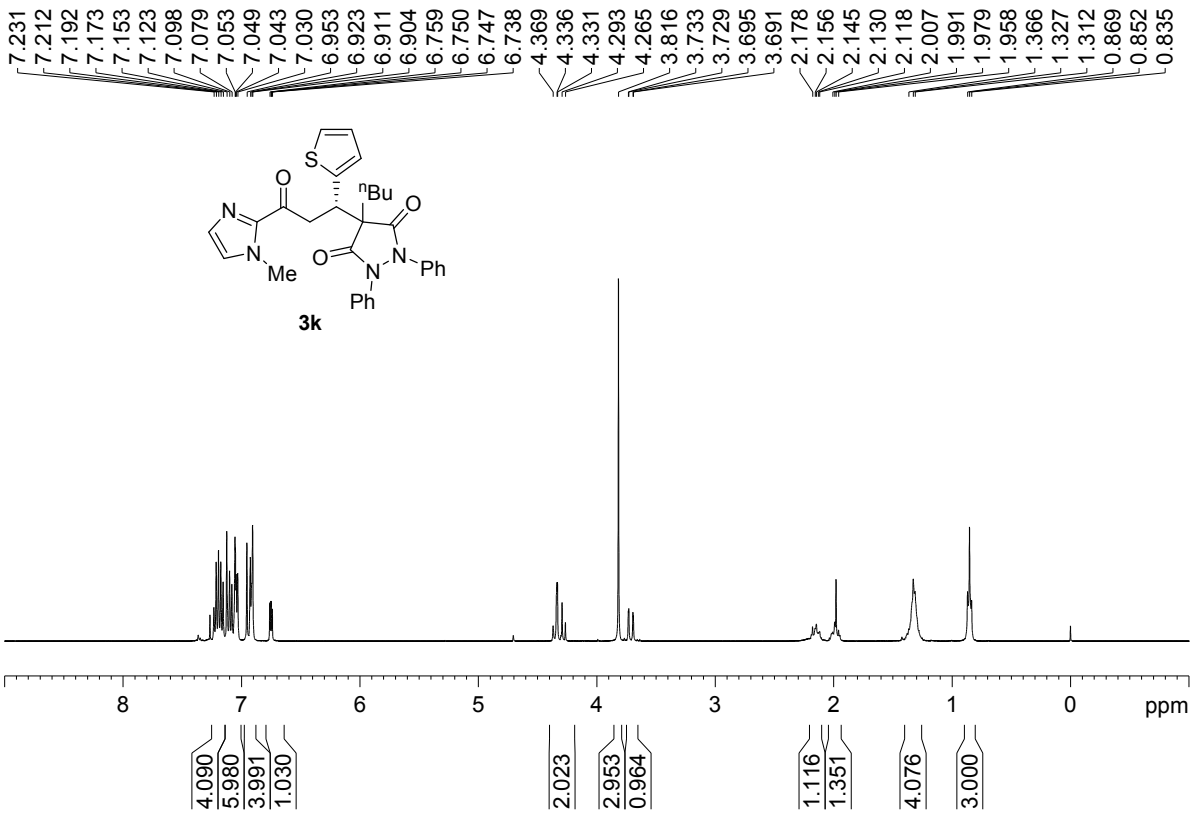
^{13}C NMR (100 MHz) spectra of **3i**



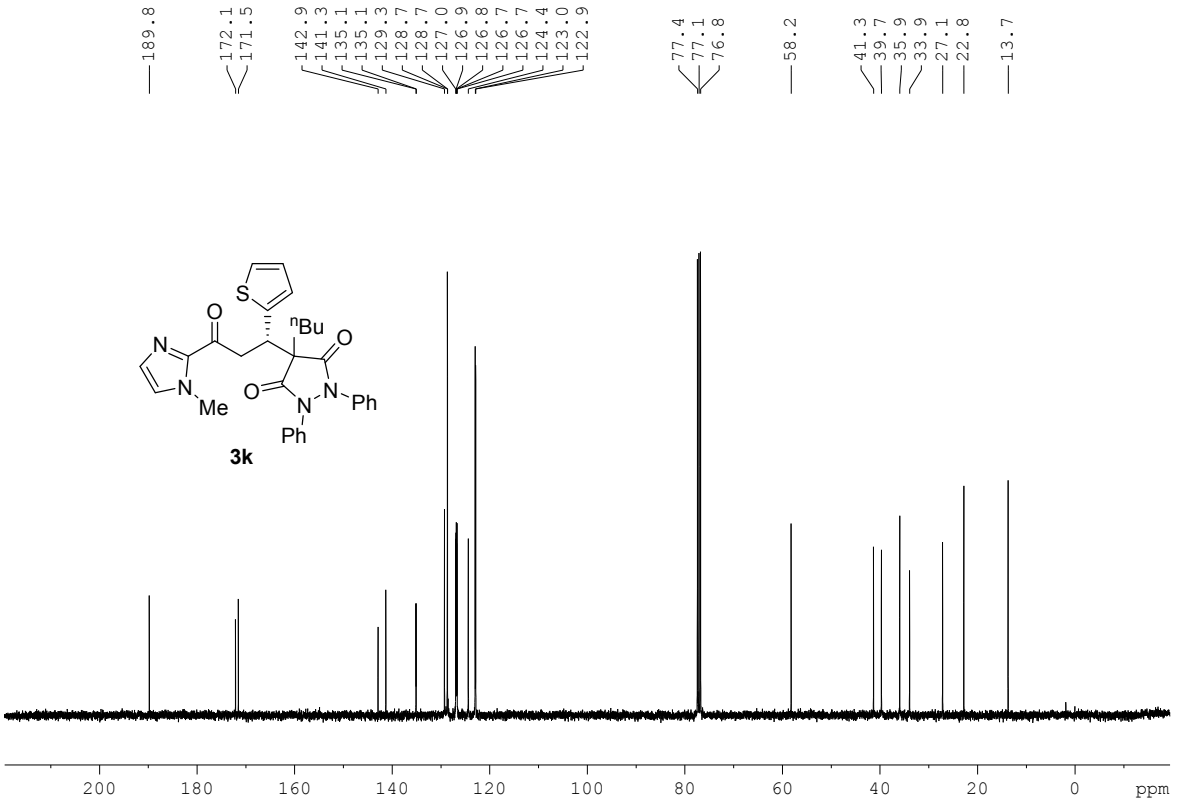
^{1}H NMR (400 MHz) spectra of **3j**



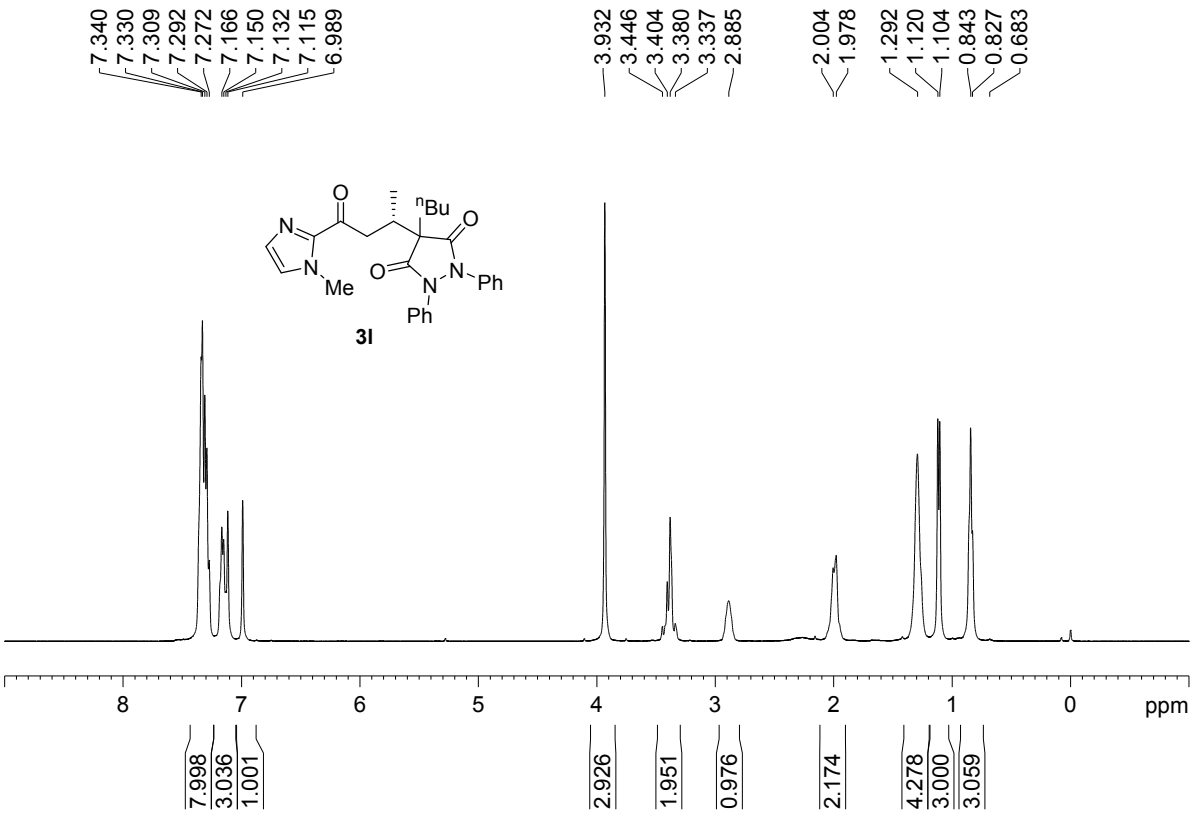
^{13}C NMR (100 MHz) spectra of **3j**



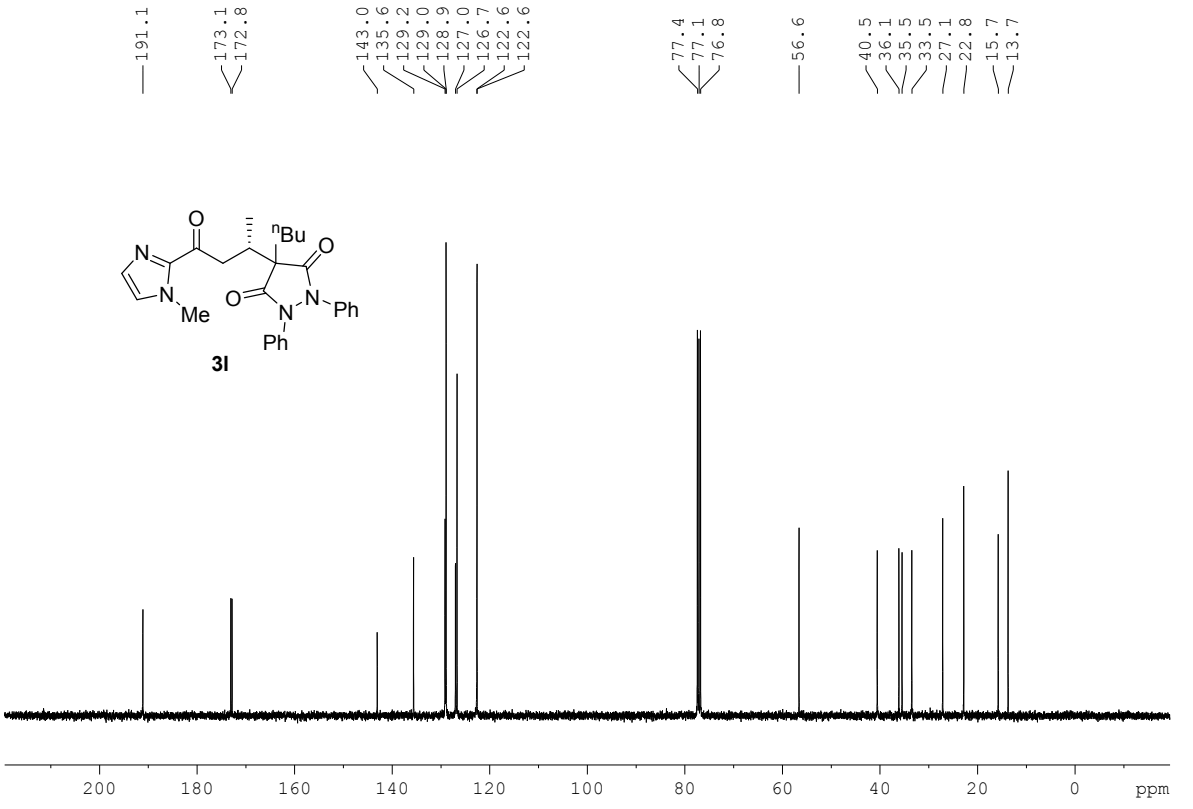
^{1}H NMR (400 MHz) spectra of **3k**



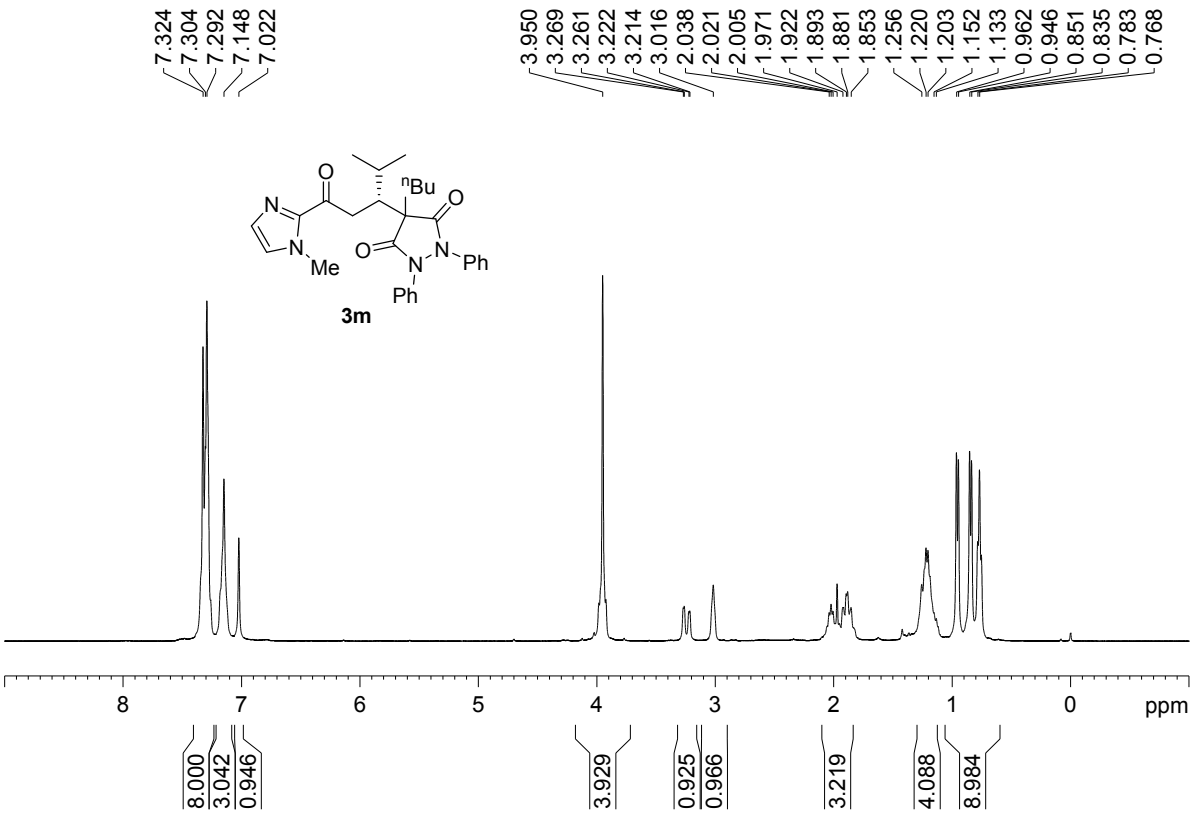
^{13}C NMR (100 MHz) spectra of **3k**



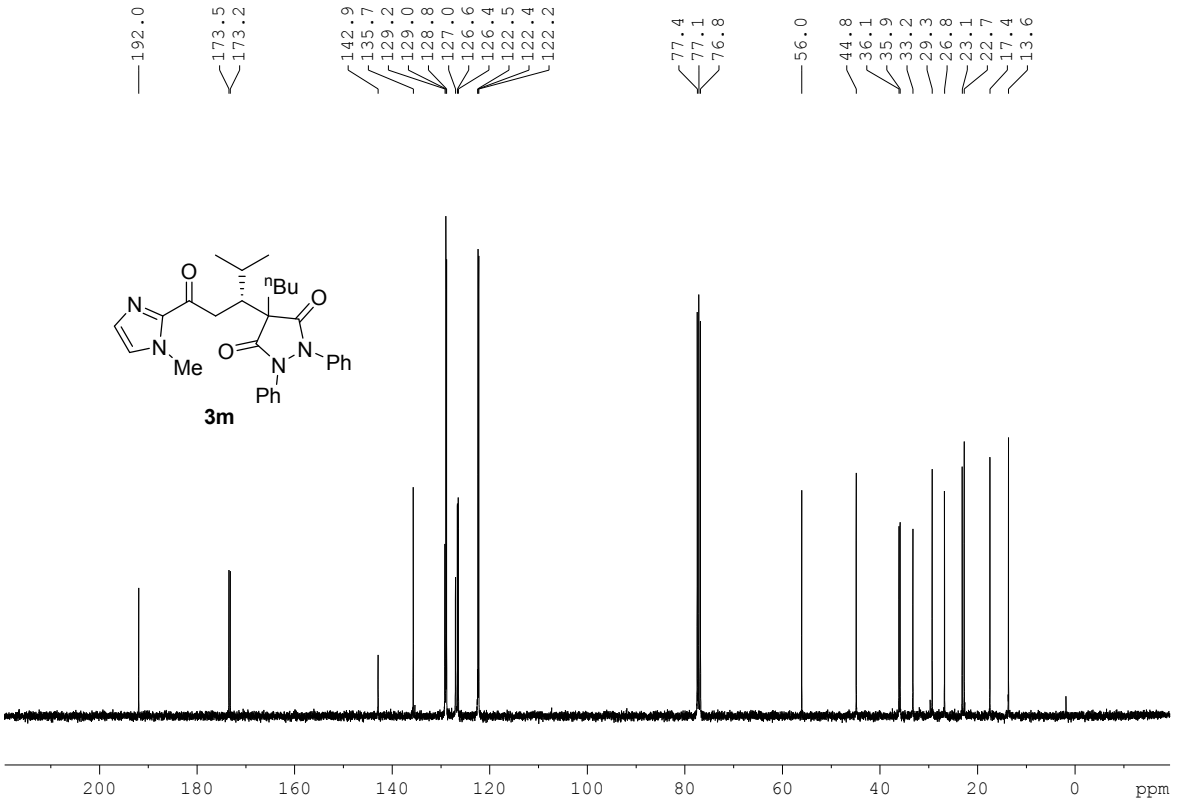
^{1}H NMR (400 MHz) spectra of **3l**



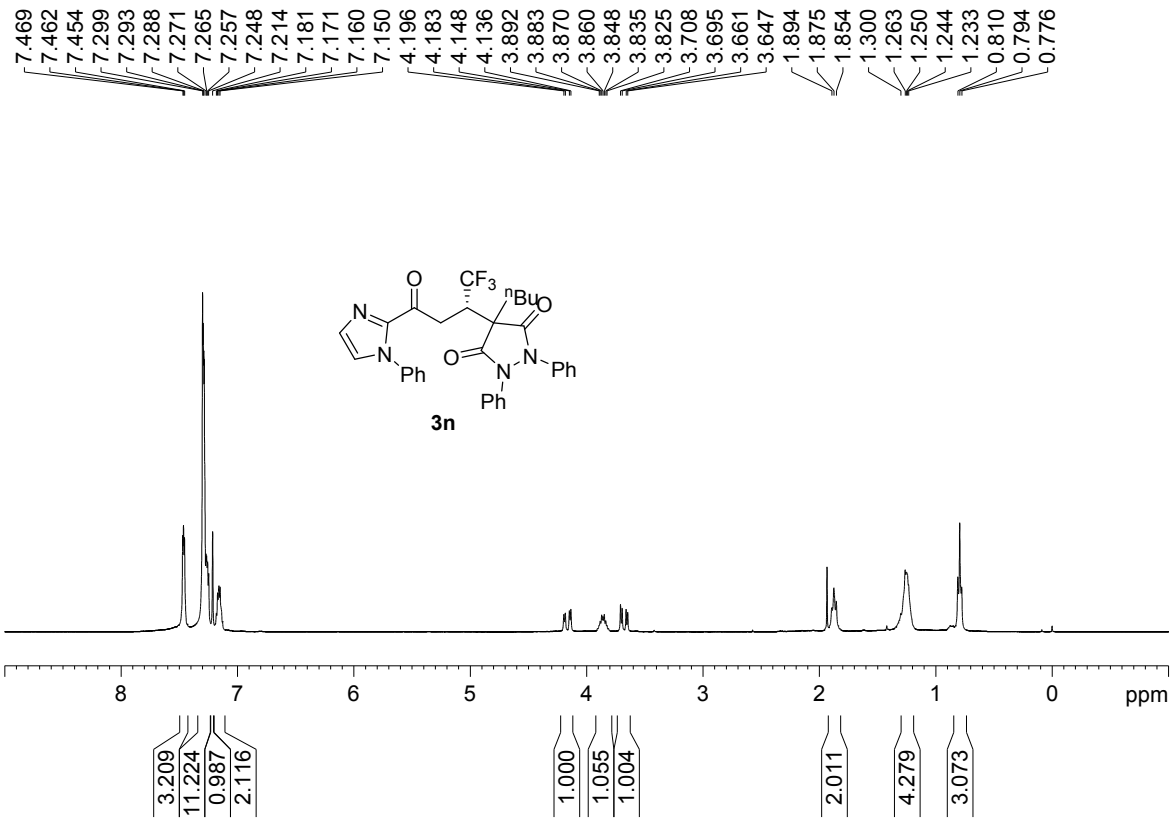
^{13}C NMR (100 MHz) spectra of **3l**



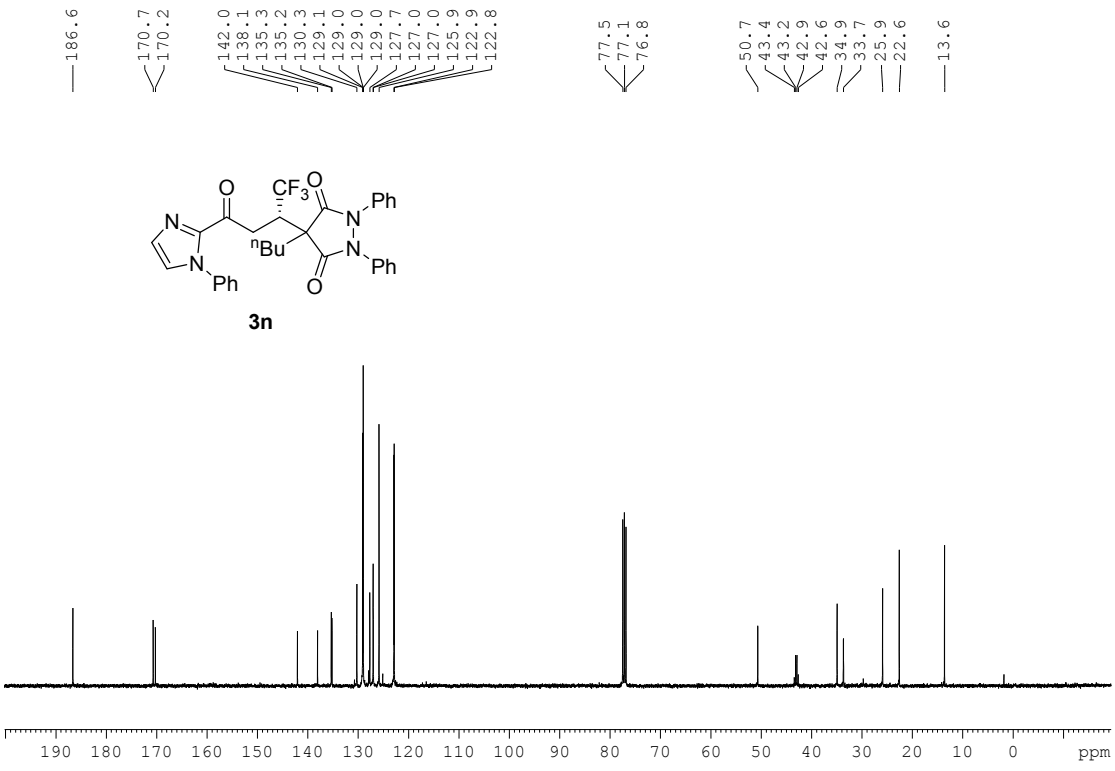
^{1}H NMR (400 MHz) spectra of **3m**



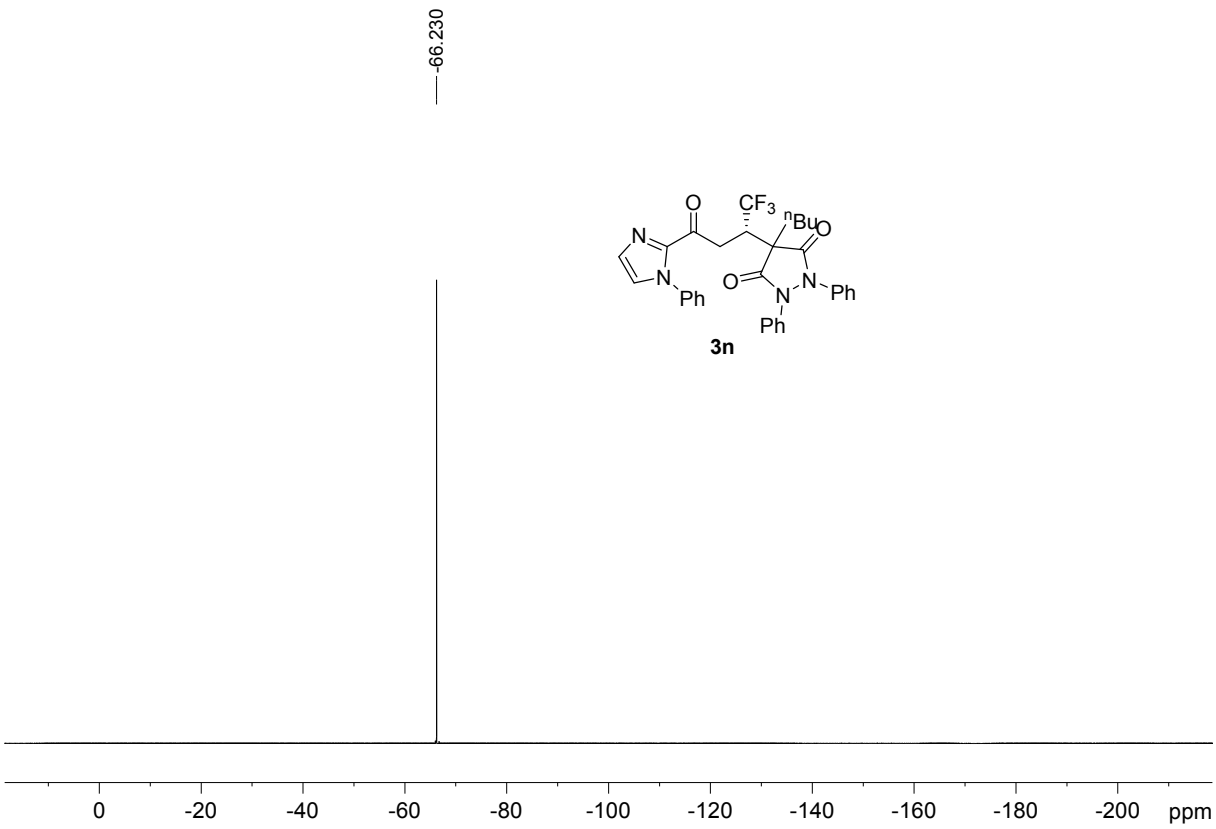
^{13}C NMR (100 MHz) spectra of **3m**



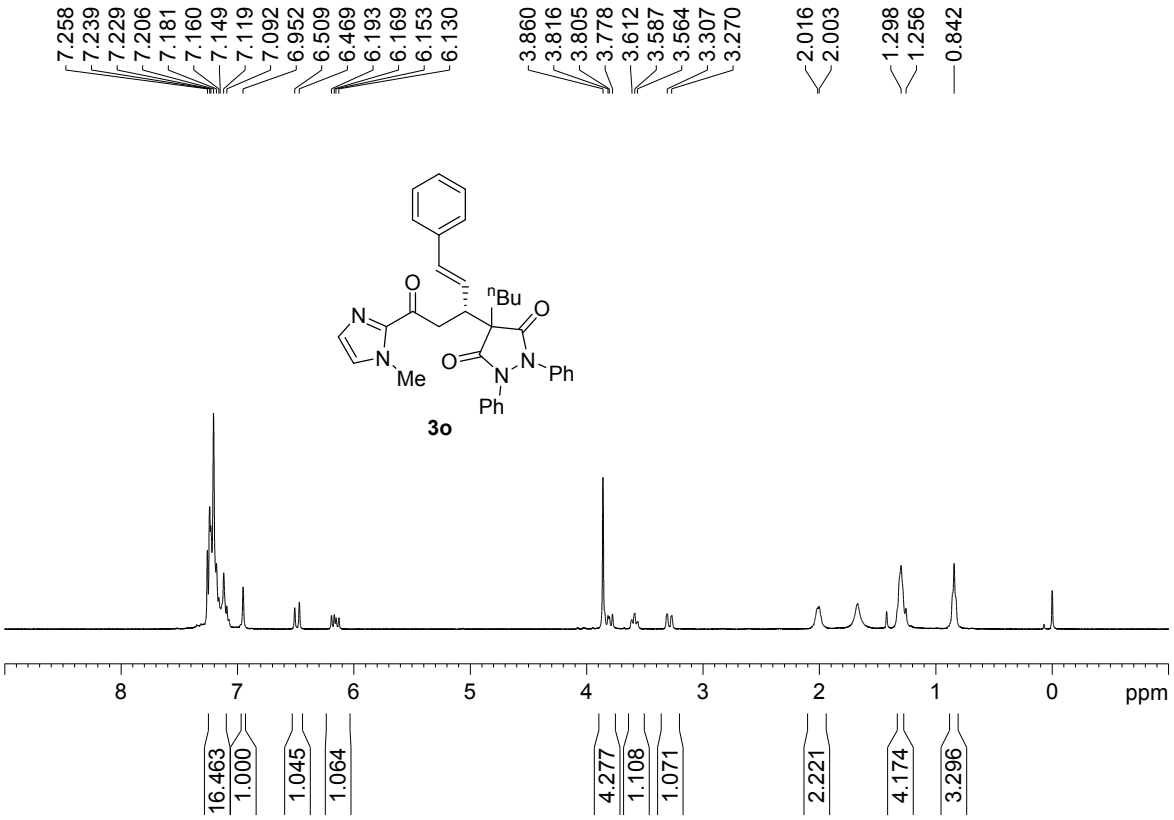
^{1}H NMR (400 MHz) spectra of **3n**



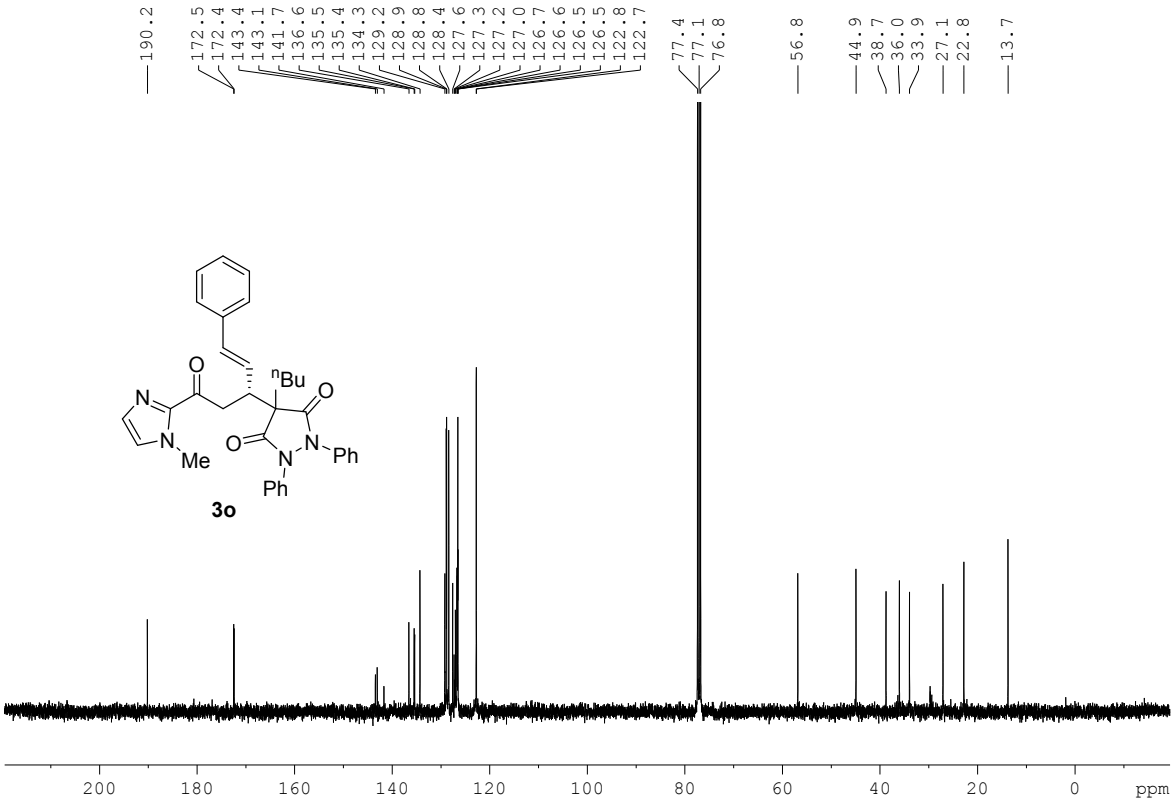
^{13}C NMR (100 MHz) spectra of **3n**



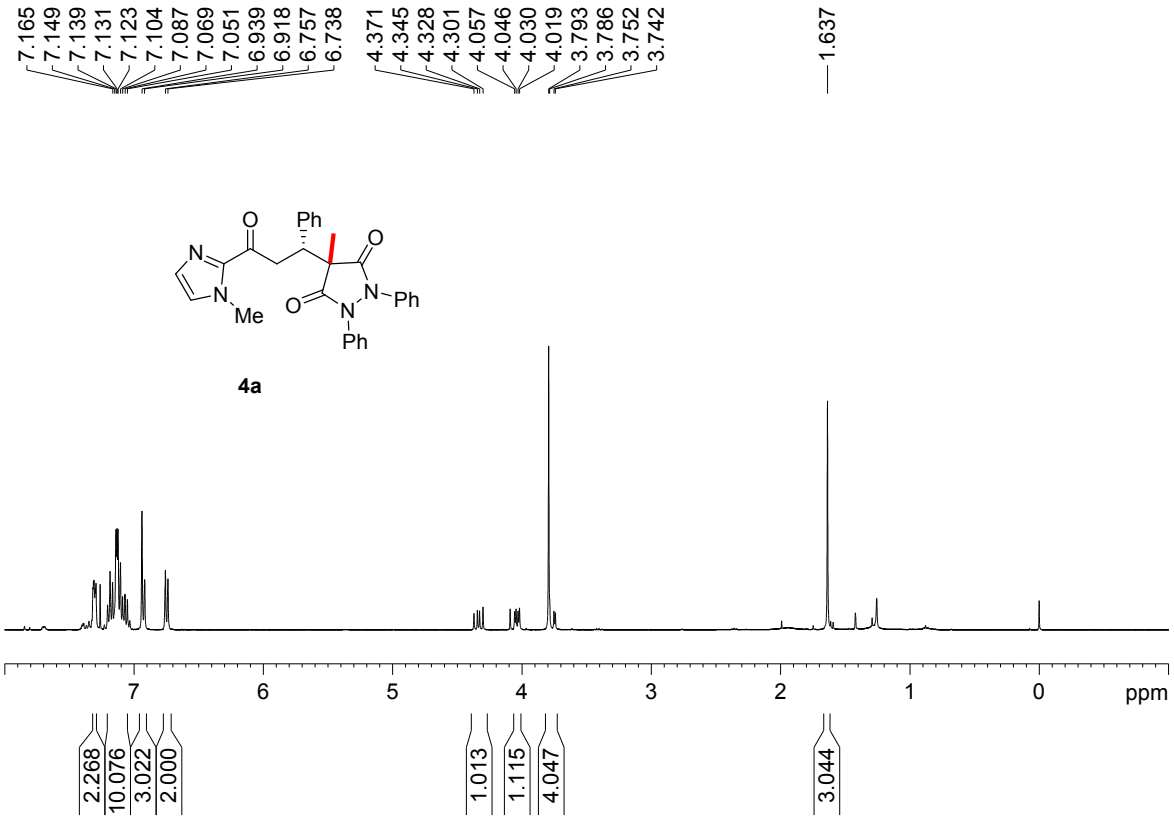
^{19}F NMR (376.4 MHz) spectra of **3n**



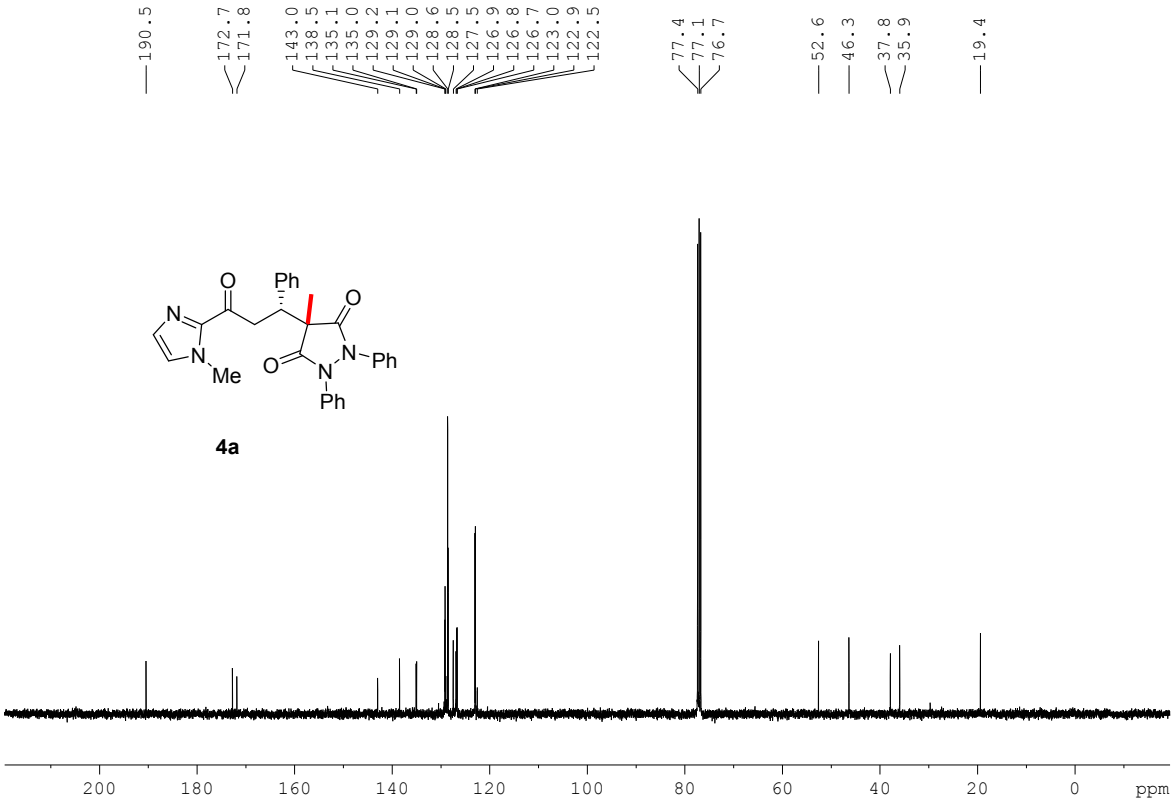
^{1}H NMR (400 MHz) spectra of **3o**



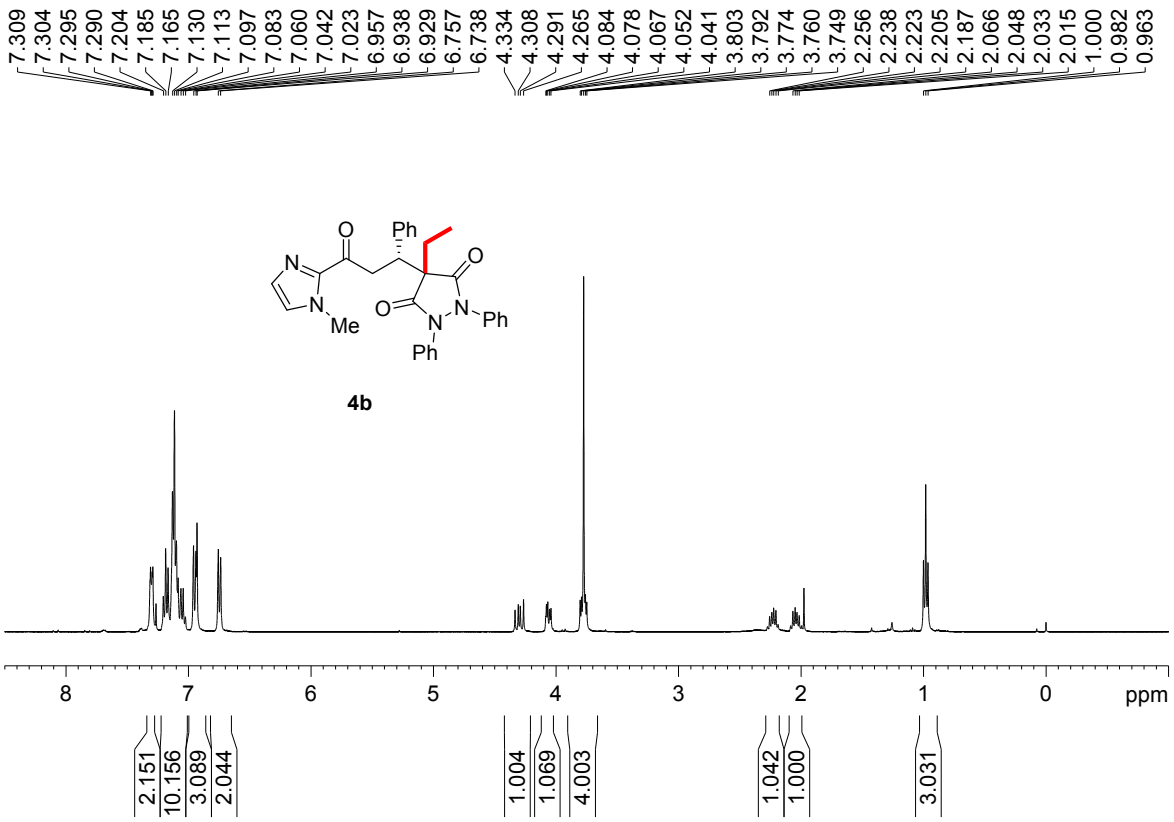
^{13}C NMR (100 MHz) spectra of **3o**



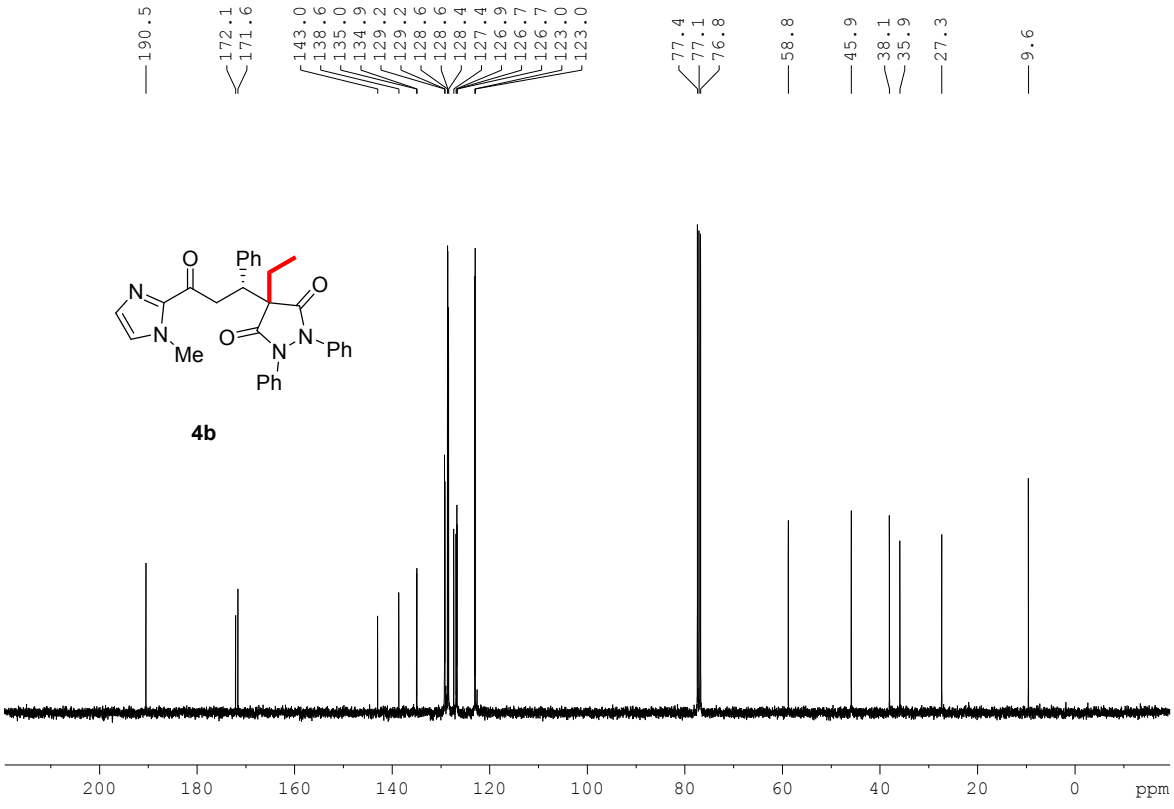
^{1}H NMR (400 MHz) spectra of **4a**



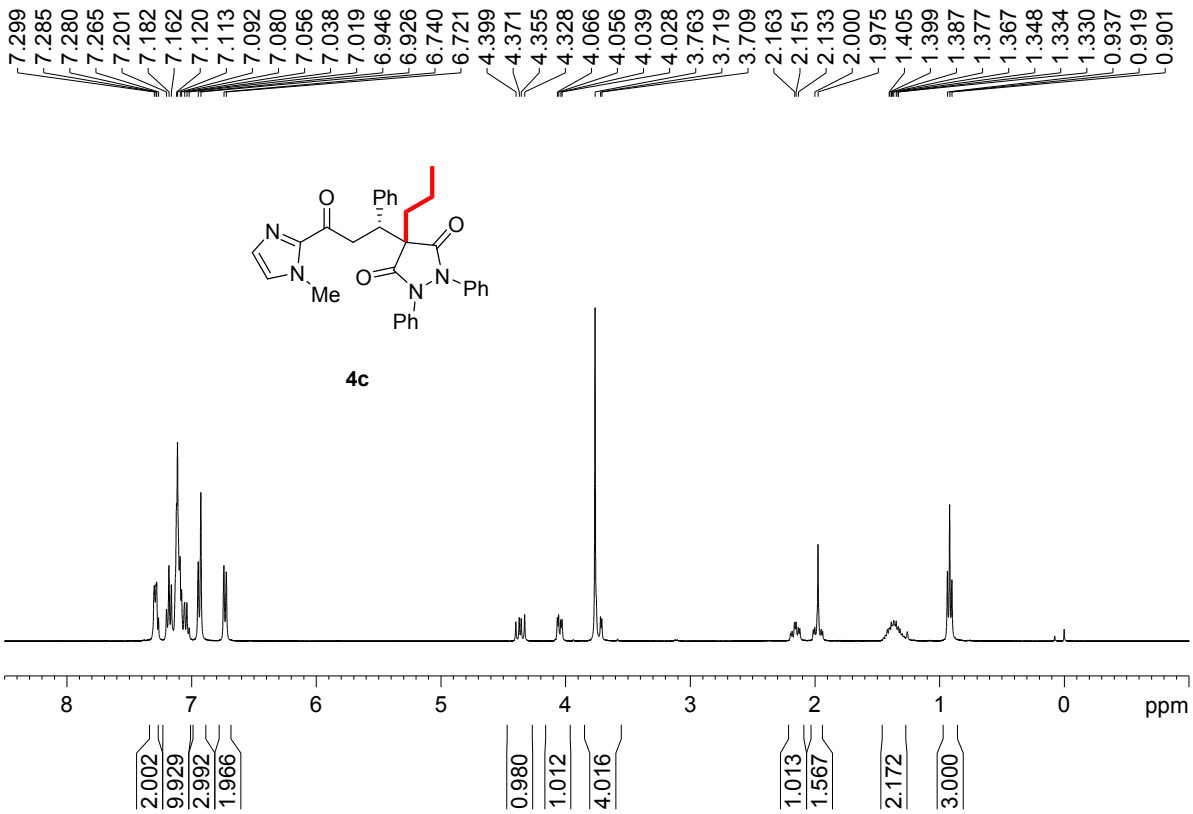
^{13}C NMR (100 MHz) spectra of **4a**



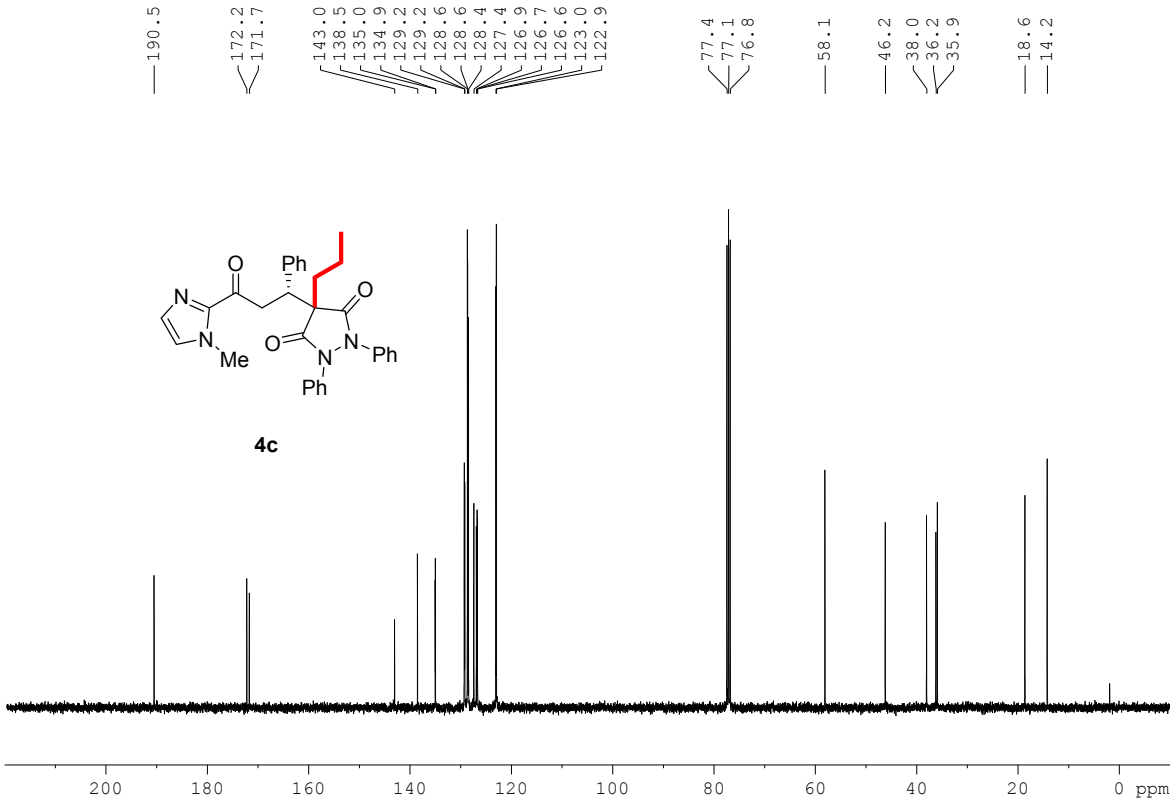
^{1}H NMR (400 MHz) spectra of **4b**



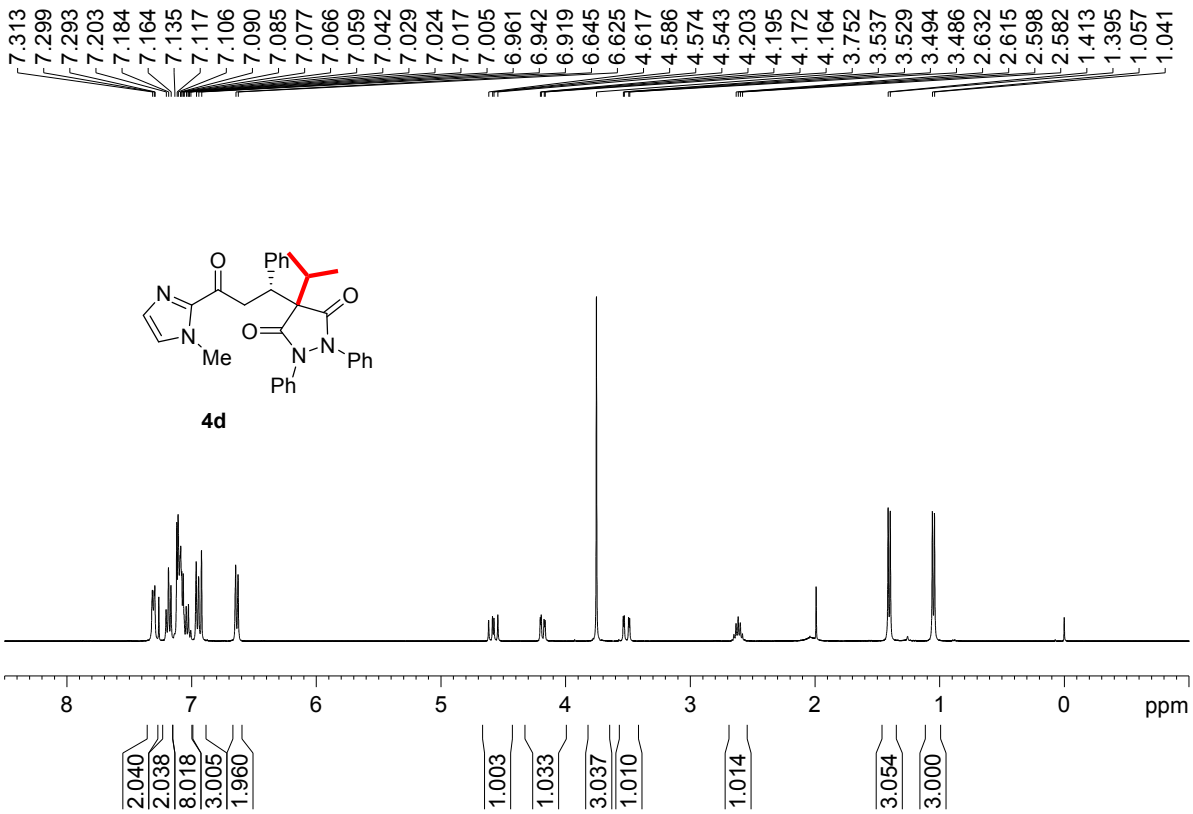
^{13}C NMR (100 MHz) spectra of **4b**



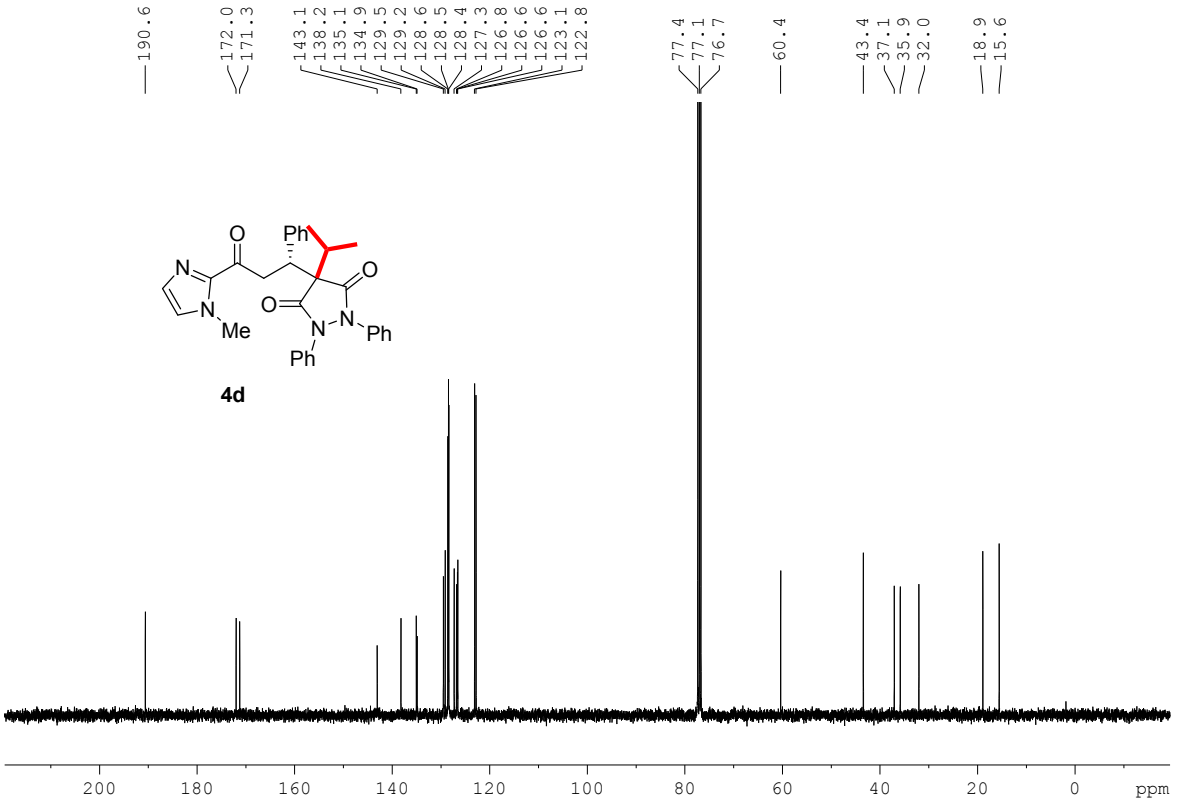
^{1}H NMR (400 MHz) spectra of **4c**



^{13}C NMR (100 MHz) spectra of **4c**



^{1}H NMR (400 MHz) spectra of **4d**



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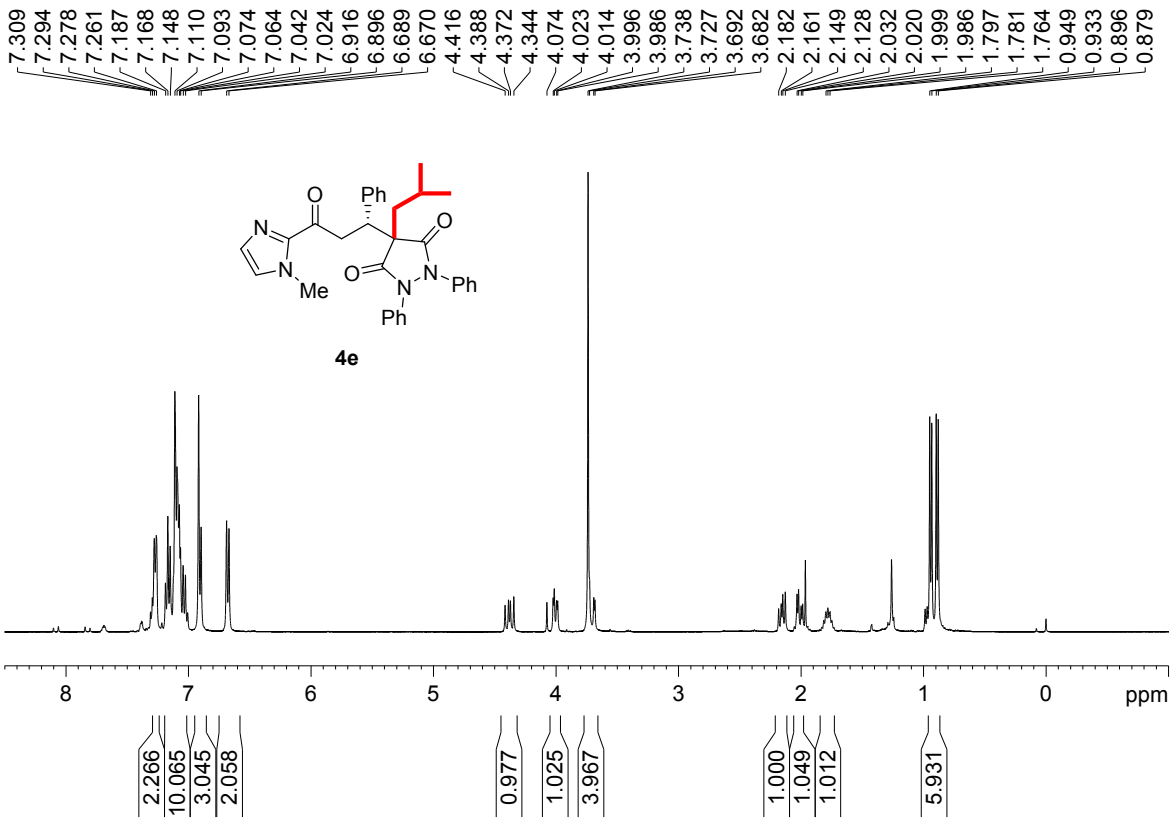
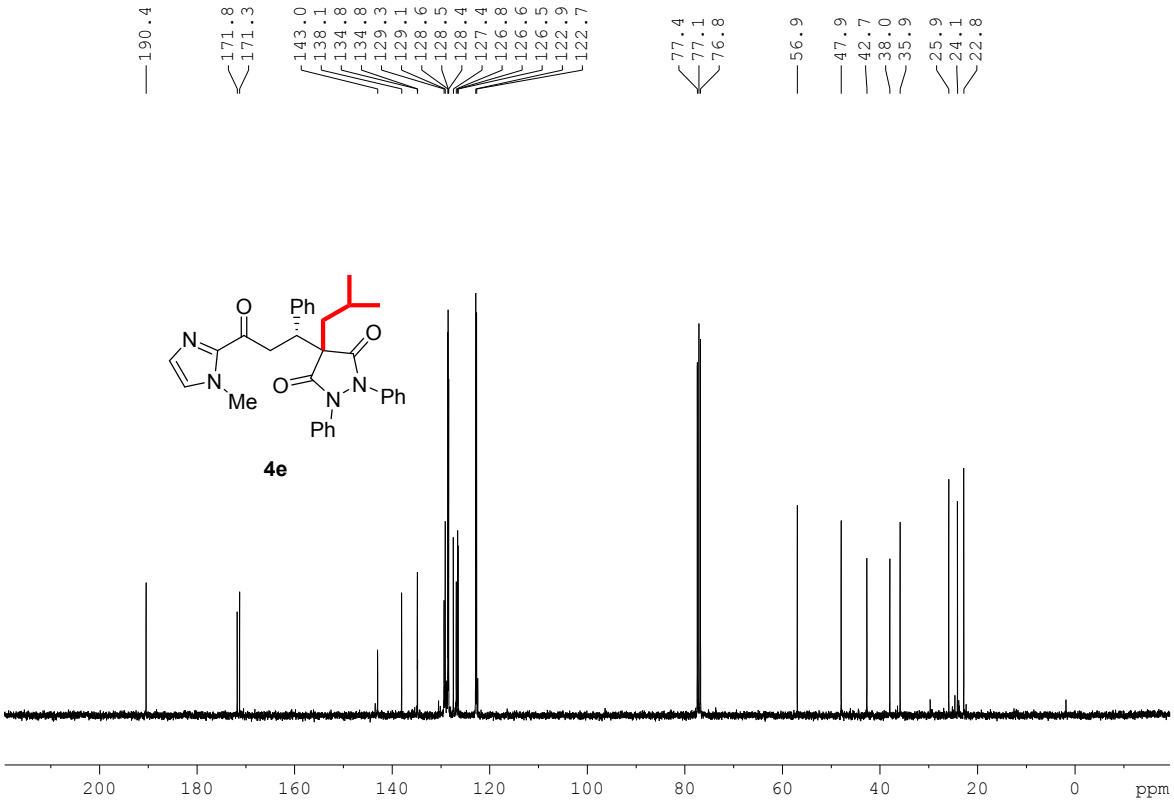
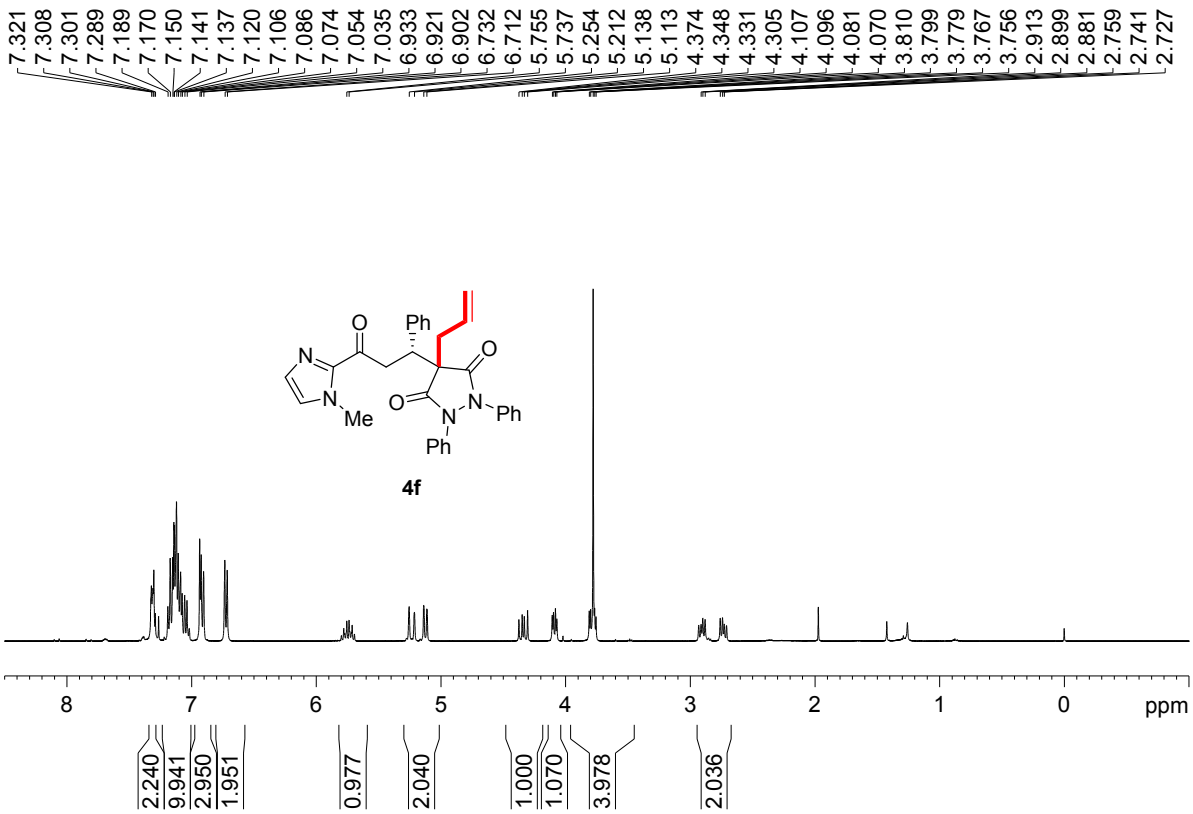


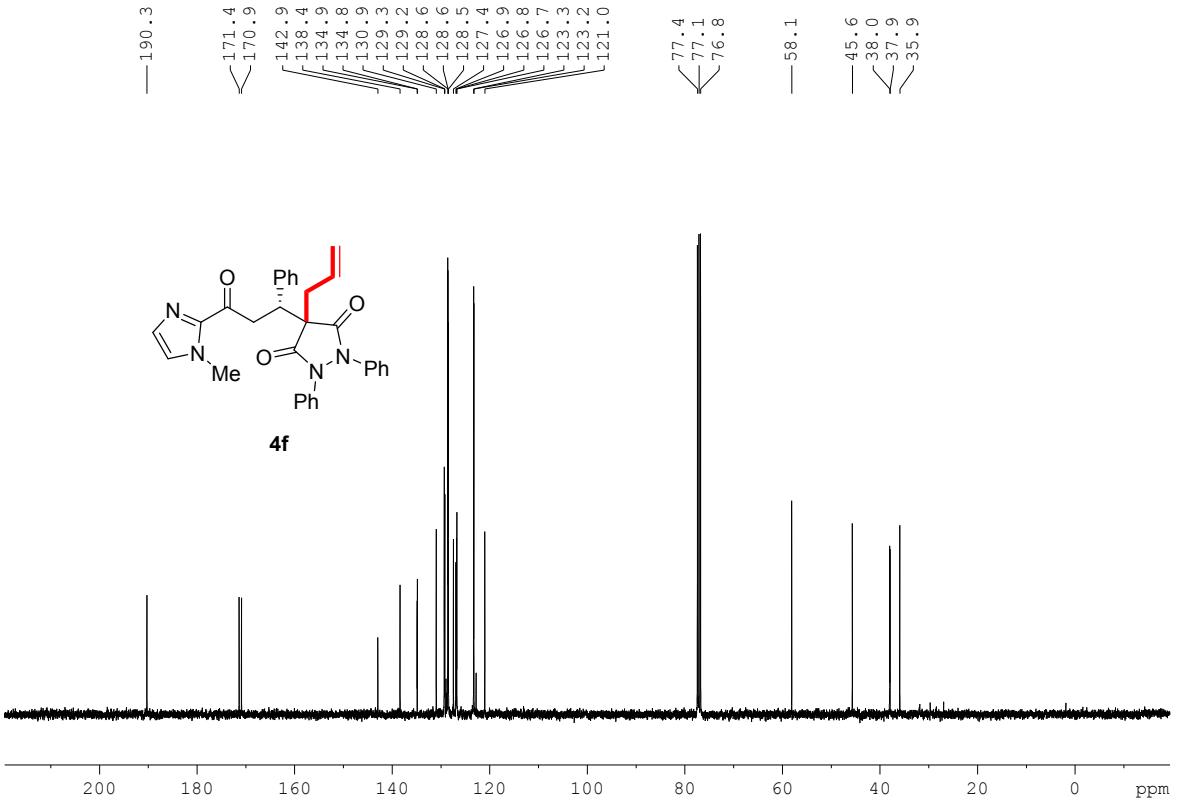
^{1}H NMR (400 MHz) spectra of **4e**



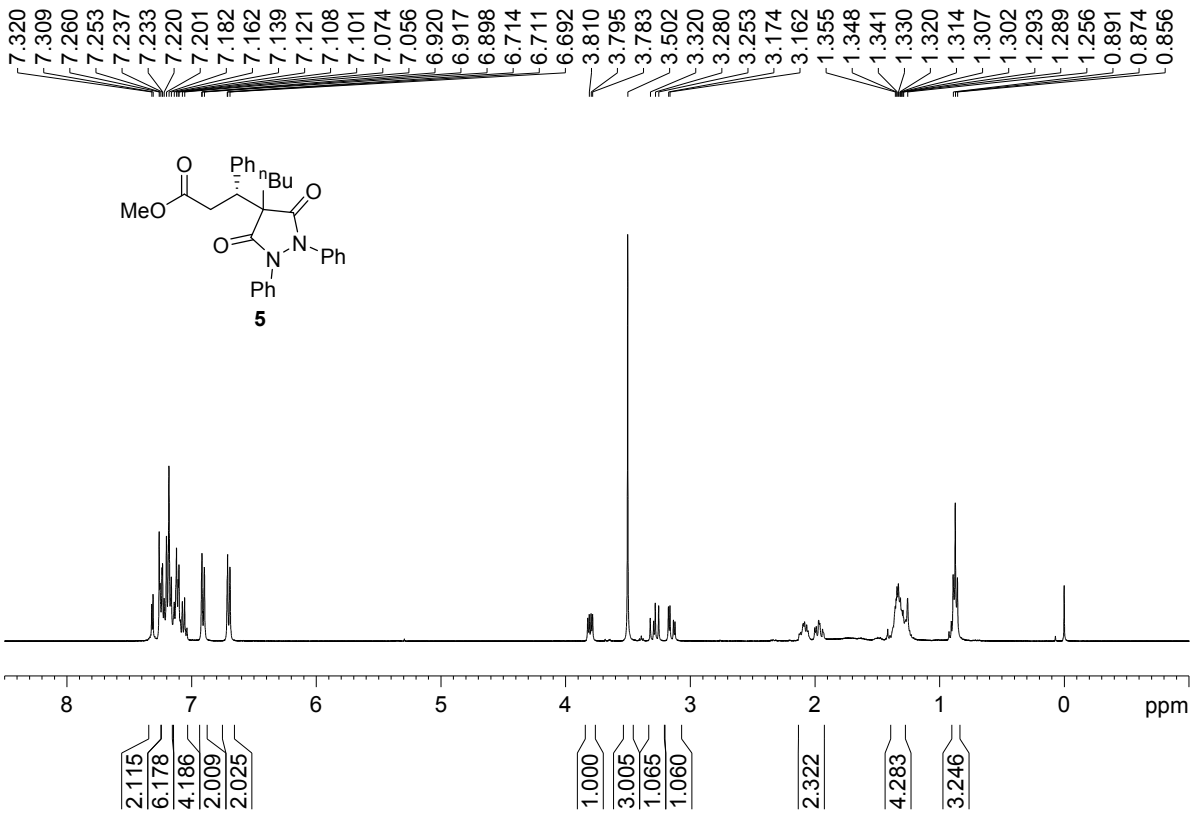
^{13}C NMR (100 MHz) spectra of **4e**



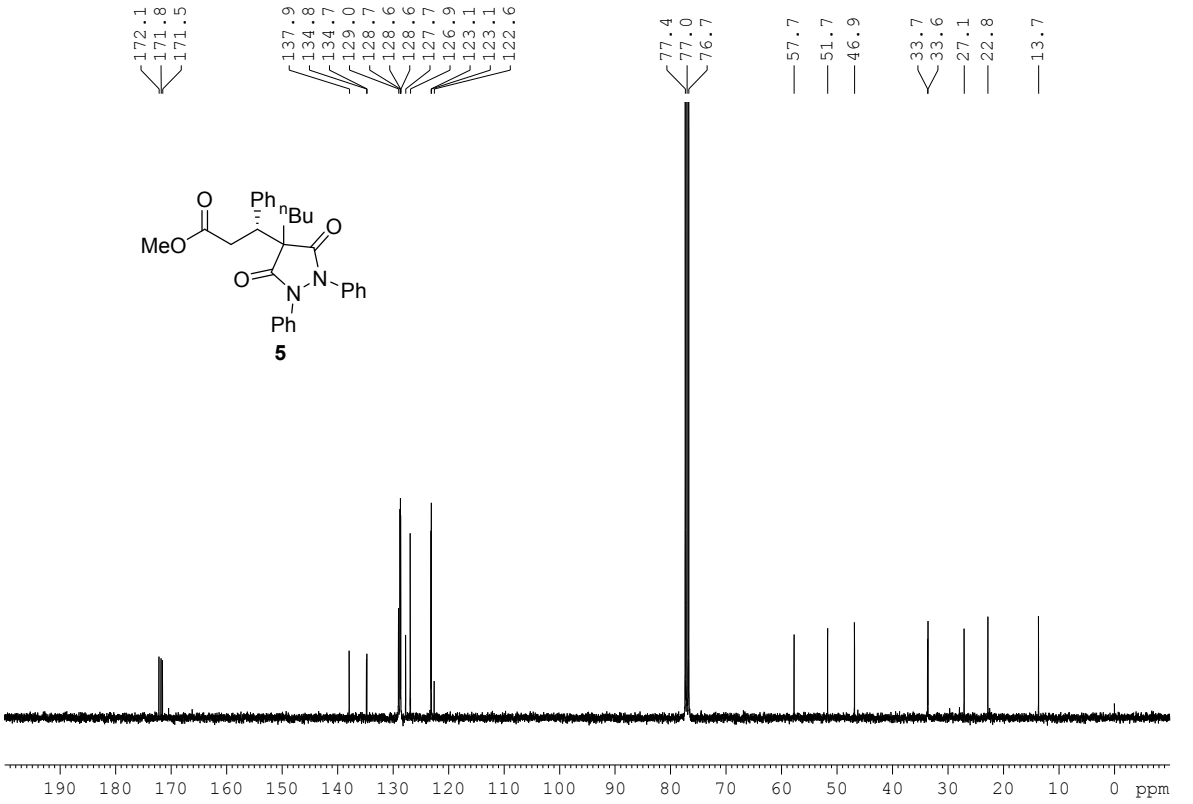
^{1}H NMR (400 MHz) spectra of **4f**



^{13}C NMR (100 MHz) spectra of **4f**



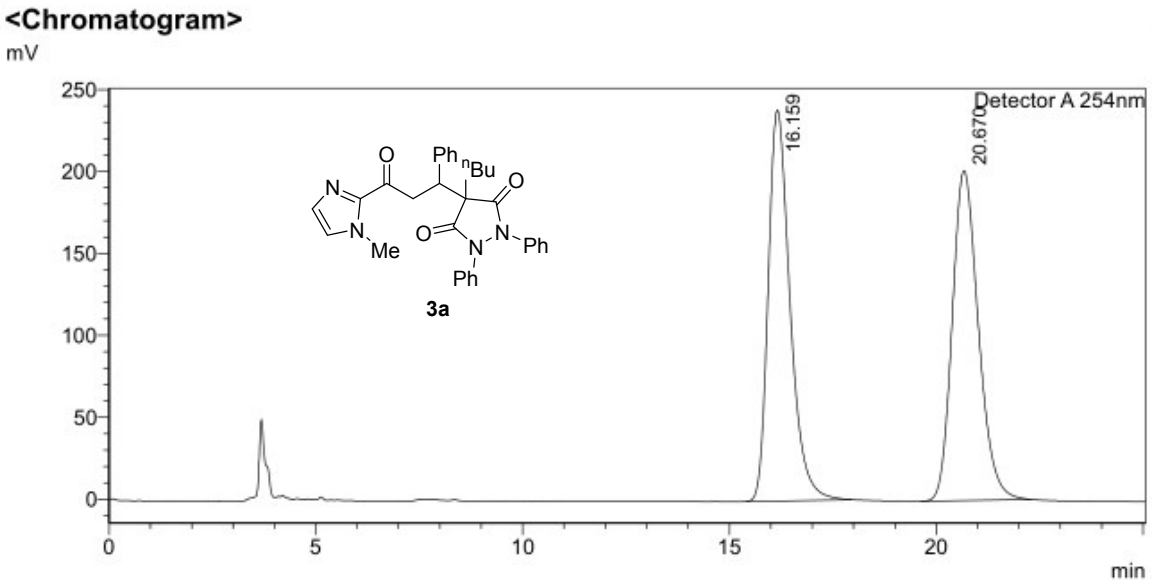
^{1}H NMR (400 MHz) spectra of **5a**



^{13}C NMR (100 MHz) spectra of **5a**

VII Chiral HPLC analysis trace

Racemic **3a**:

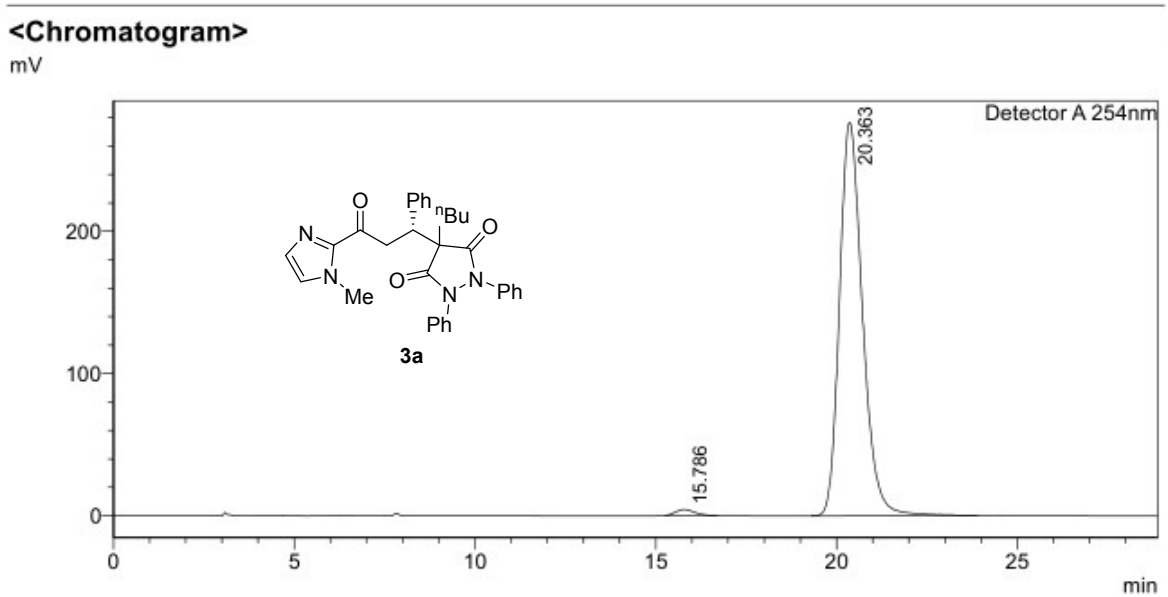


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.159	8732773	238532	49.729		M	
2	20.670	8827874	201384	50.271		M	
Total		17560647	439916				

Chiral **3a**:



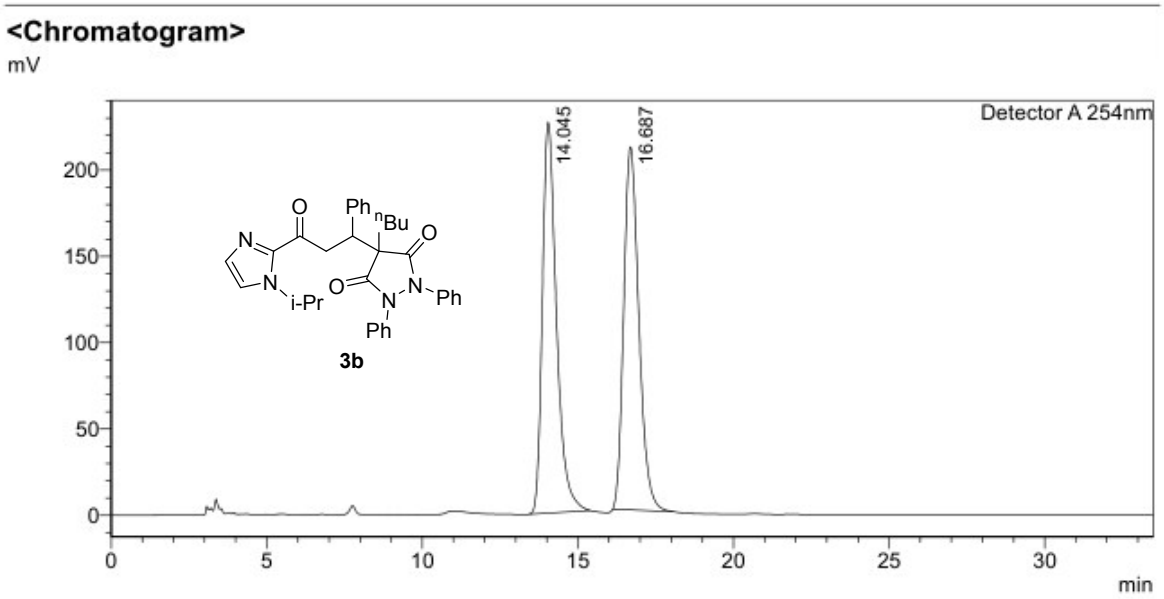
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	15.786	154677	4230	1.247		M	
2	20.363	12246388	276389	98.753		M	
Total		12401065	280619				

HPLC traces of racemic **3a** and chiral **3a**. Area integration = 97.506% = 98% ee.

Racemic **3b**:

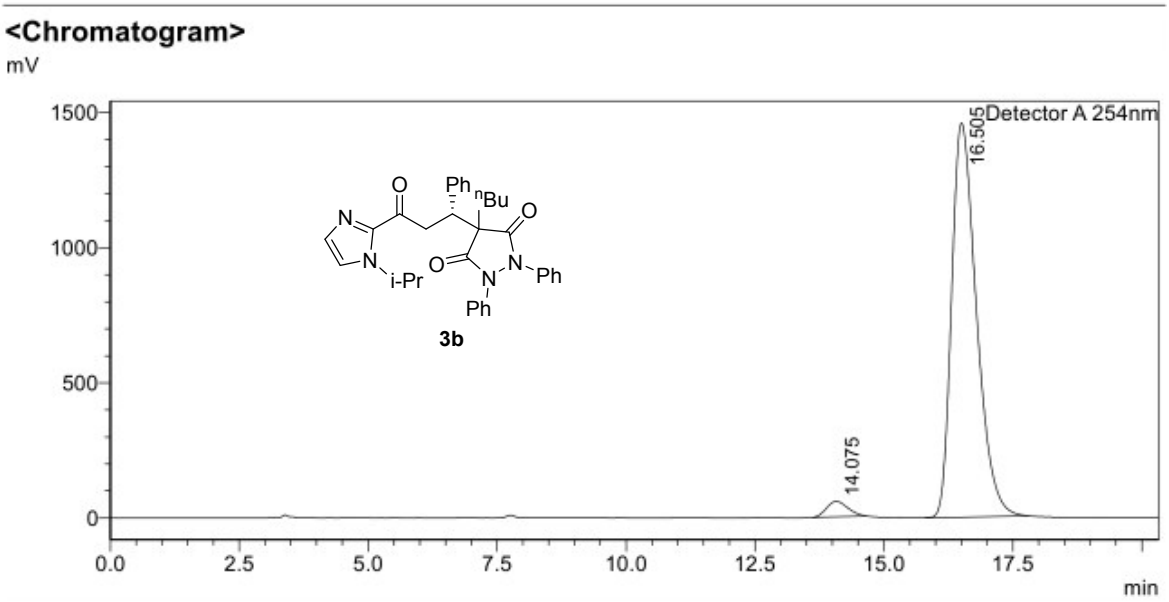


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.045	7116829	226343	50.091		M	
2	16.687	7090925	210167	49.909		M	
Total		14207754	436510				

Chiral **3b**:



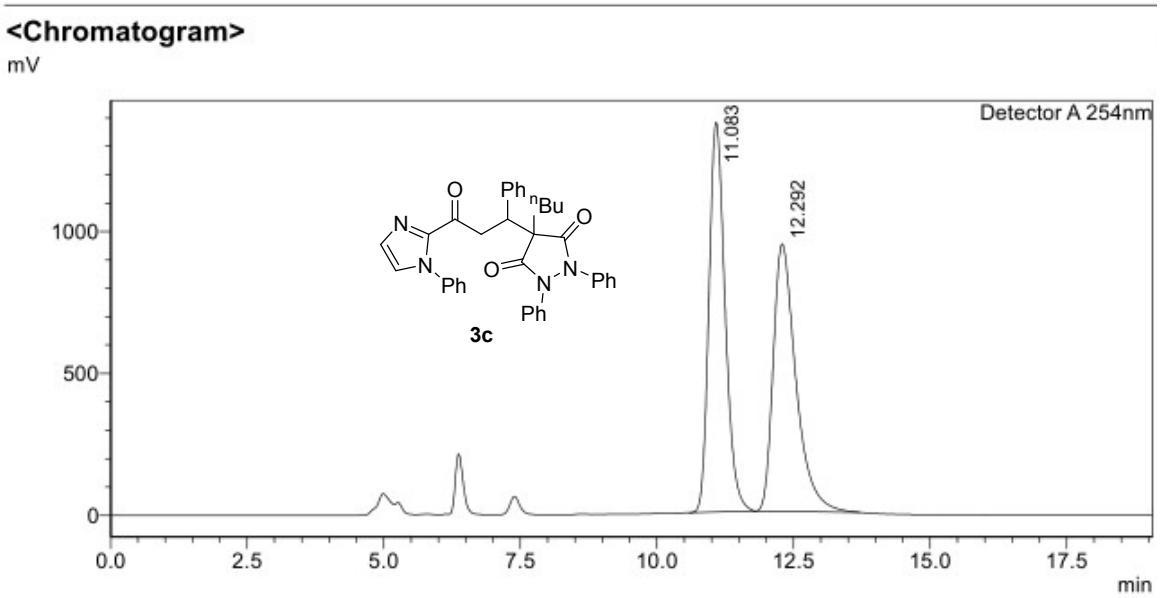
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.075	1641472	57102	3.260		M	
2	16.505	48716609	1458055	96.740		M	
Total		50358081	1515157				

HPLC traces of racemic **3a** and chiral **3a**. Area integration = 93.48% = 93% ee.

Racemic **3c**:

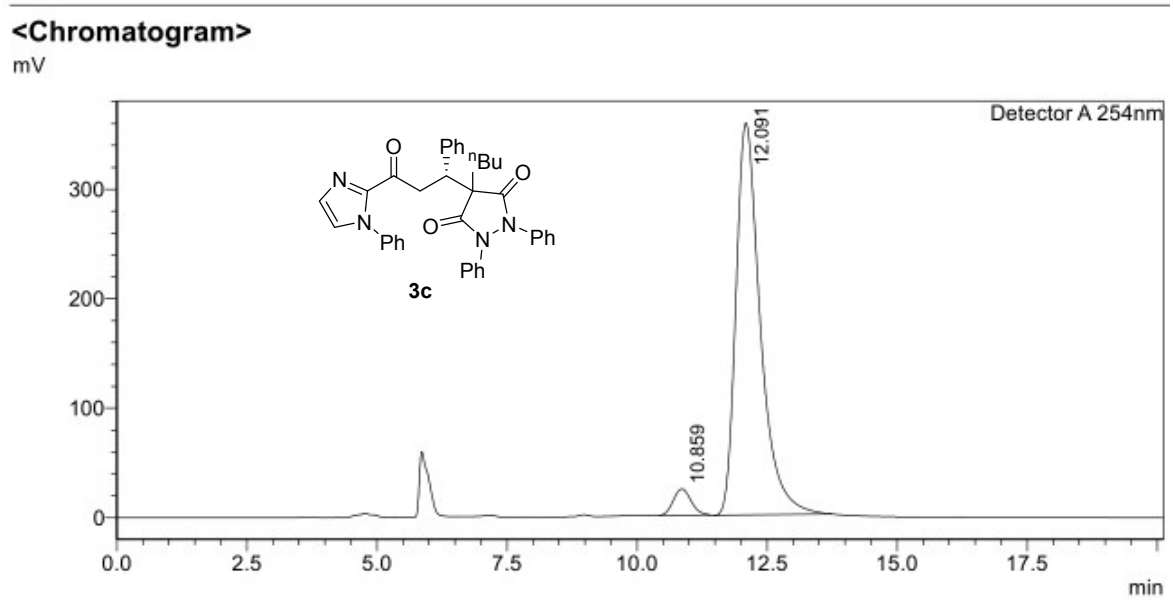


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.083	28145096	1371958	50.826		M	
2	12.292	27230641	941133	49.174		M	
Total		55375737	2313091				

Chiral **3c**:



<Peak Table>

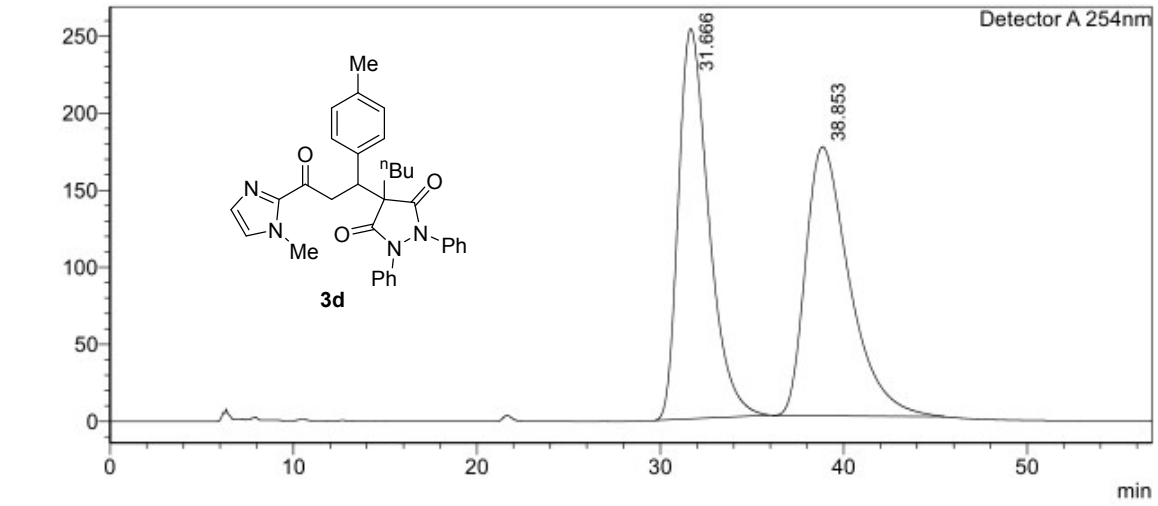
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.859	565397	23952	4.615		M	
2	12.091	11684717	358184	95.385		M	
Total		12250114	382136				

HPLC traces of racemic **3c** and chiral **3c**. Area integration = 90.77% = 91% ee.

Racemic **3d**:

<Chromatogram>



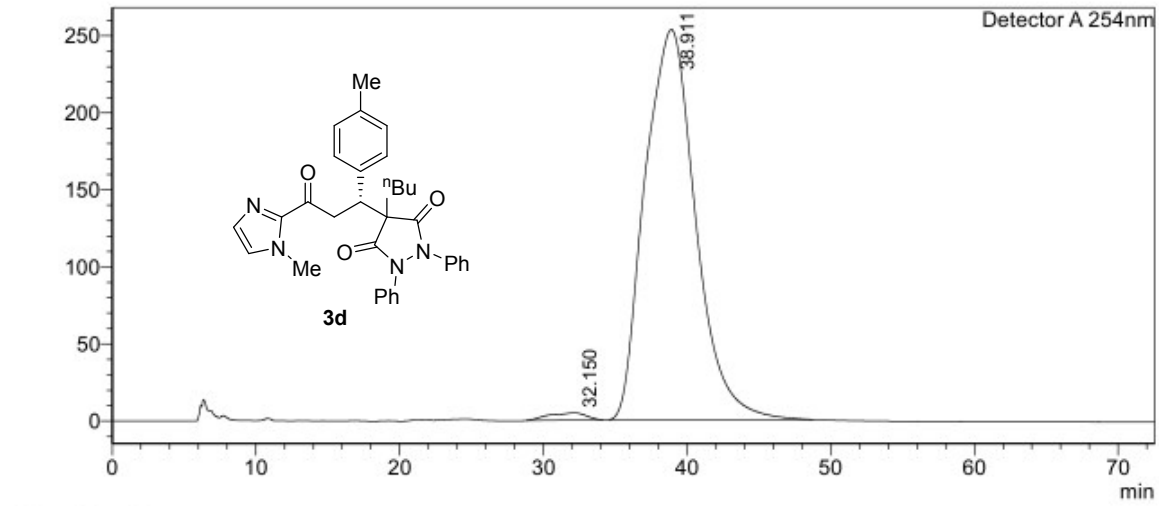
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	31.666	29131827	253109	50.059		M	
2	38.853	29062677	174495	49.941		M	
Total		58194504	427604				

Chiral **3d**:

<Chromatogram>



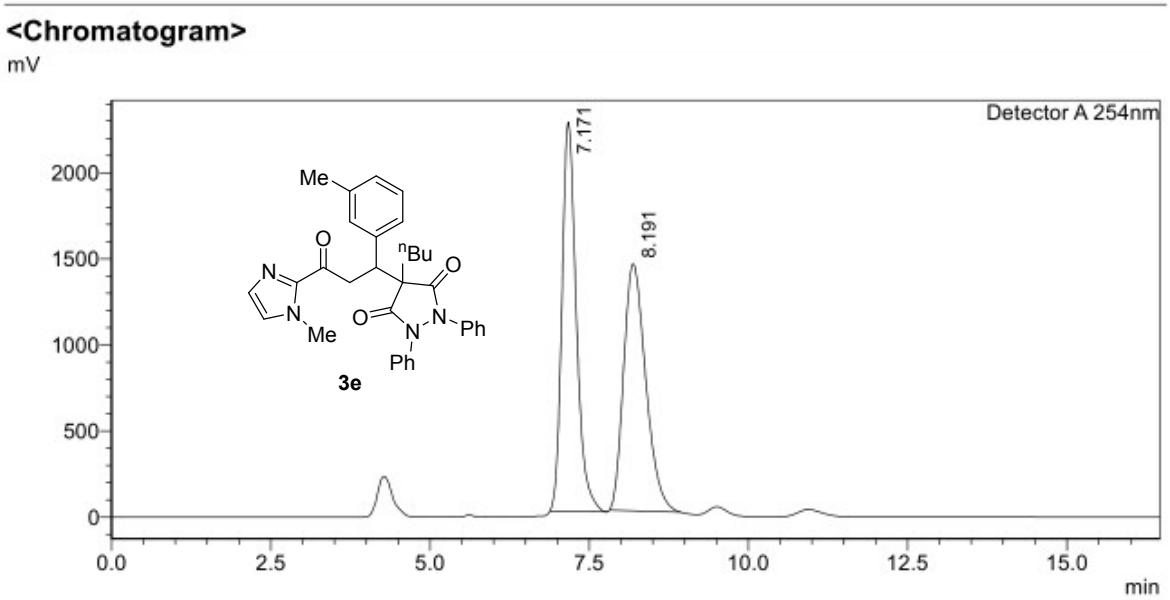
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	32.150	866105	4748	1.374		M	
2	38.911	62159911	253291	98.626		M	
Total		63026015	258039				

HPLC traces of racemic **3d** and chiral **3d**. Area integration = 97.252% = 97% ee.

Racemic **3e**:

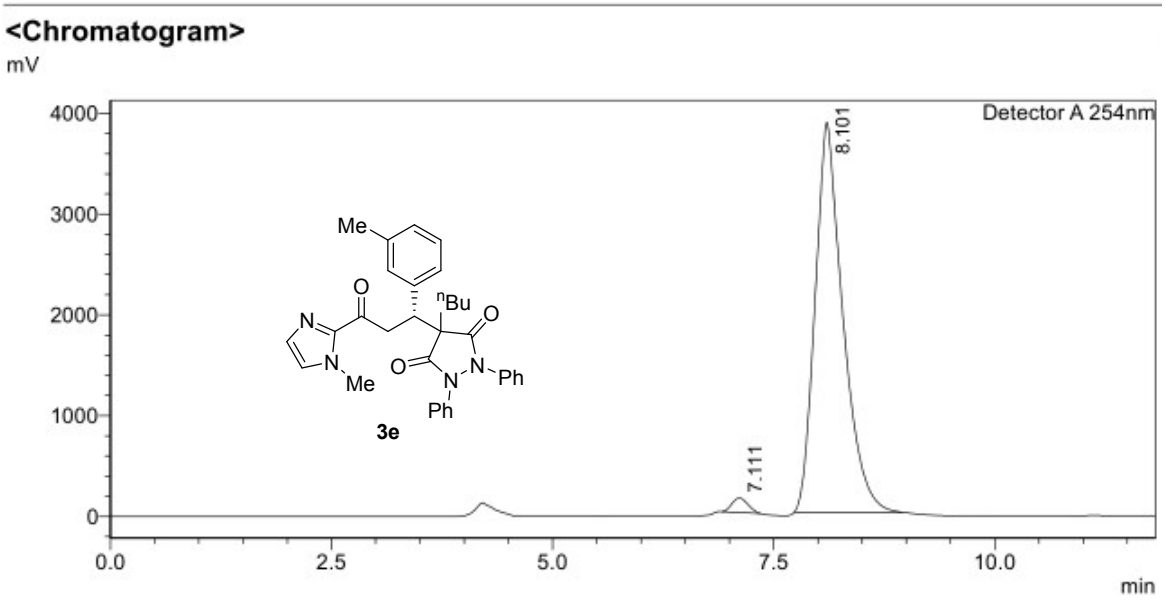


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.171	35293163	2257529	50.435		M	
2	8.191	34683696	1434033	49.565		M	
Total		69976859	3691562				

Chiral **3e**:



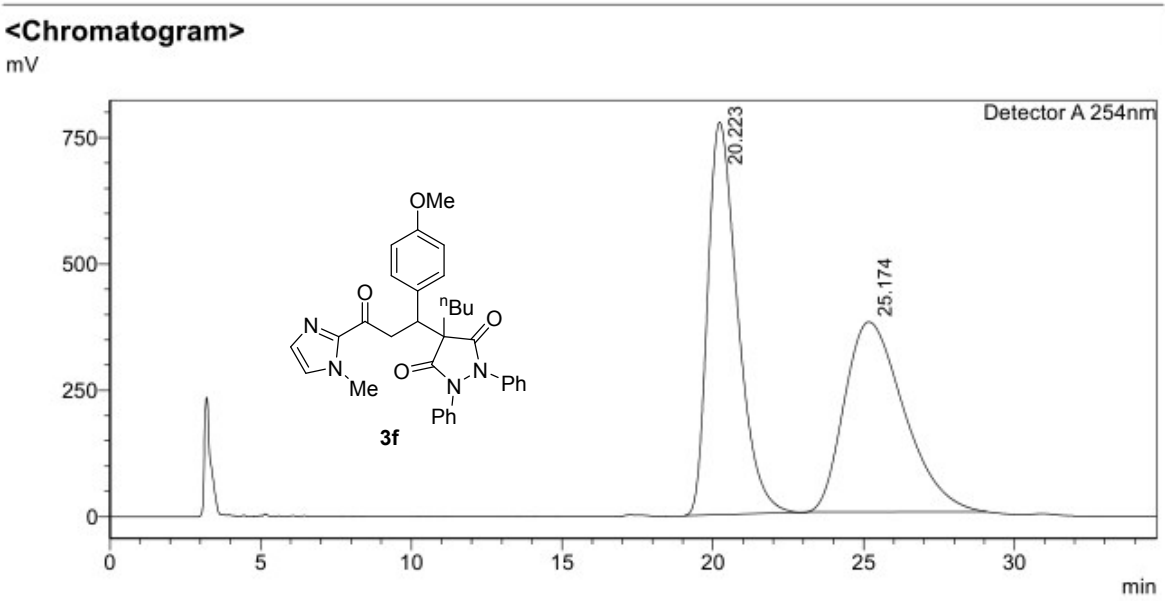
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.111	1790183	142574	2.083		M	
2	8.101	84172613	3867566	97.917		M	
Total		85962797	4010140				

HPLC traces of racemic **3e** and chiral **3e**. Area integration = 95.834% = 96% ee.

Racemic **3f**:

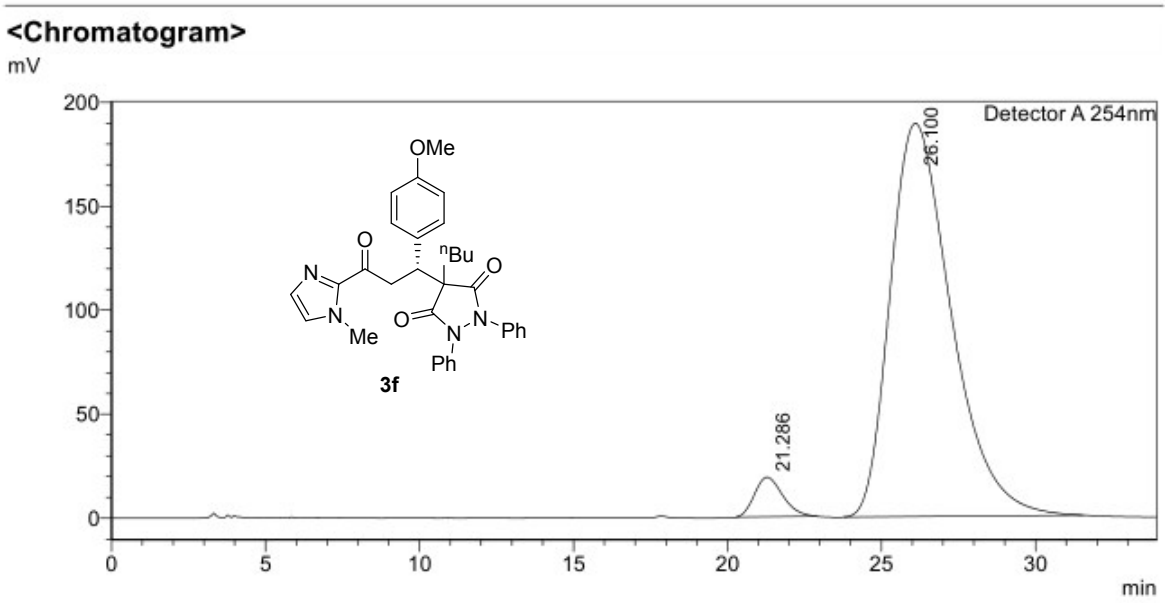


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	20.223	53617326	776380	50.852		M	
2	25.174	51820545	375999	49.148		M	
Total		105437871	1152378				

Chiral **3f**:



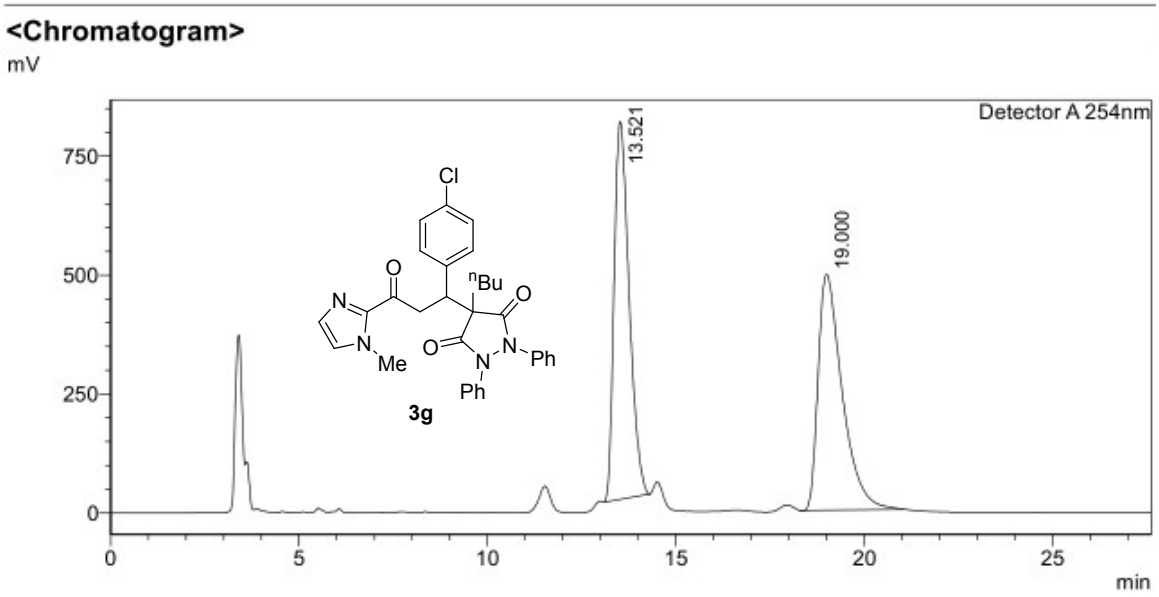
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	21.286	1219908	19060	4.467		M	
2	26.100	26089169	189138	95.533		M	
Total		27309077	208198				

HPLC traces of racemic **3f** and chiral **3f**. Area integration = 91.066% = 91% ee.

Racemic **3g**:

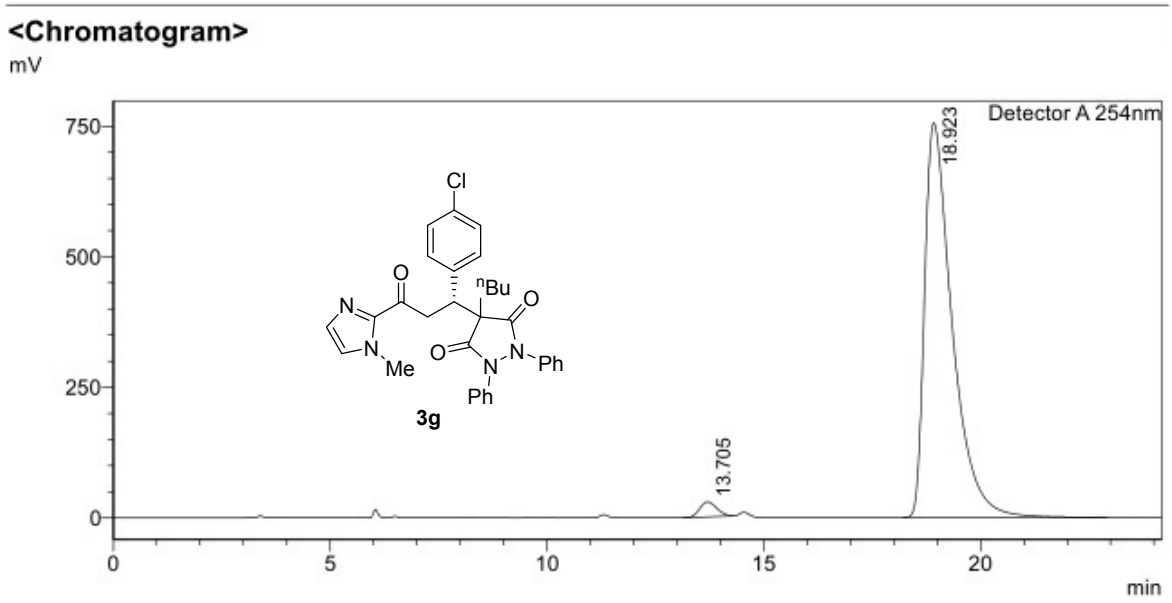


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.521	21985028	794026	49.936		M	
2	19.000	22041510	495733	50.064		M	
Total		44026538	1289759				

Chiral **3g**:



<Peak Table>

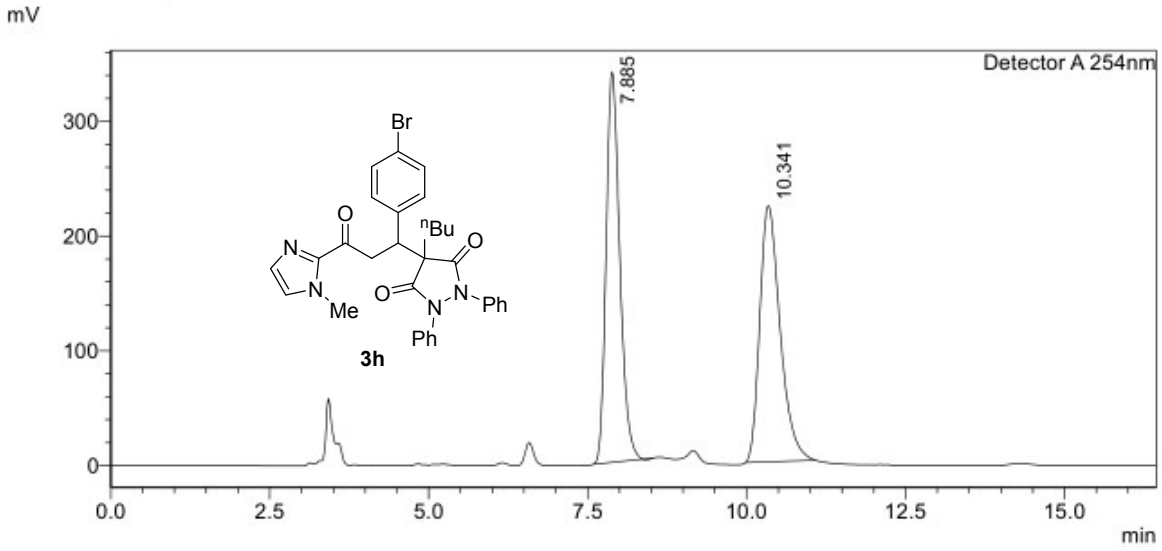
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.705	782334	28654	2.288		M	
2	18.923	33407387	756125	97.712		M	
Total		34189722	784779				

HPLC traces of racemic **3g** and chiral **3g**. Area integration = 95.424% = 95% ee.

Racemic **3h**:

<Chromatogram>



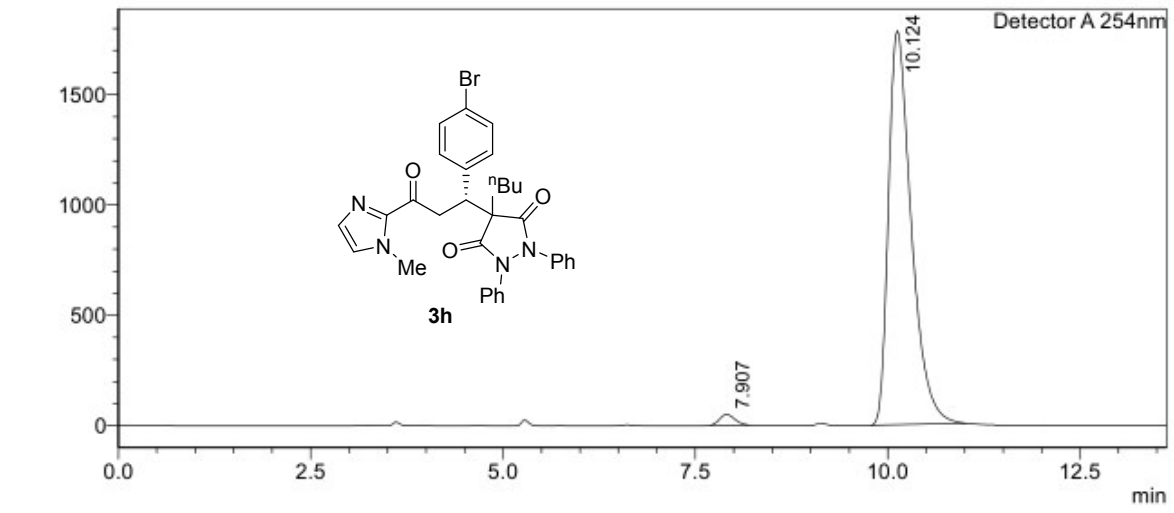
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.885	5069621	340046	50.458		M	
2	10.341	4977543	223395	49.542		M	
Total		10047164	563442				

Chiral **3h**:

<Chromatogram>



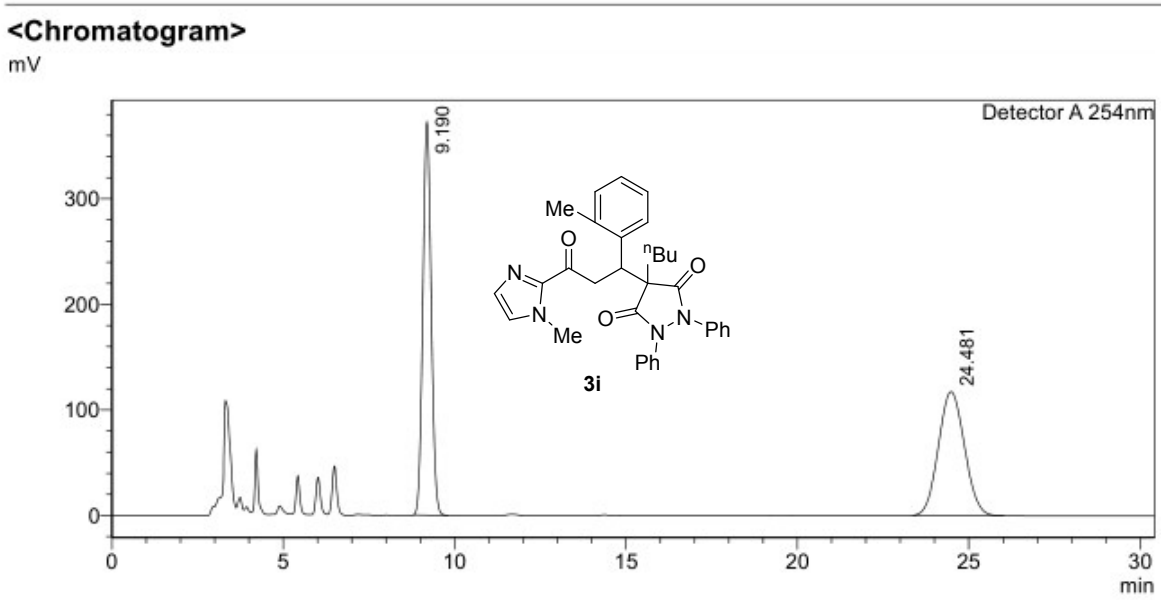
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.907	654040	48743	1.749		M	
2	10.124	36743296	1784325	98.251		M	
Total		37397335	1833068				

HPLC traces of racemic **3h** and chiral **3h**. Area integration = 96.502% = 97% ee.

Racemic **3i**:

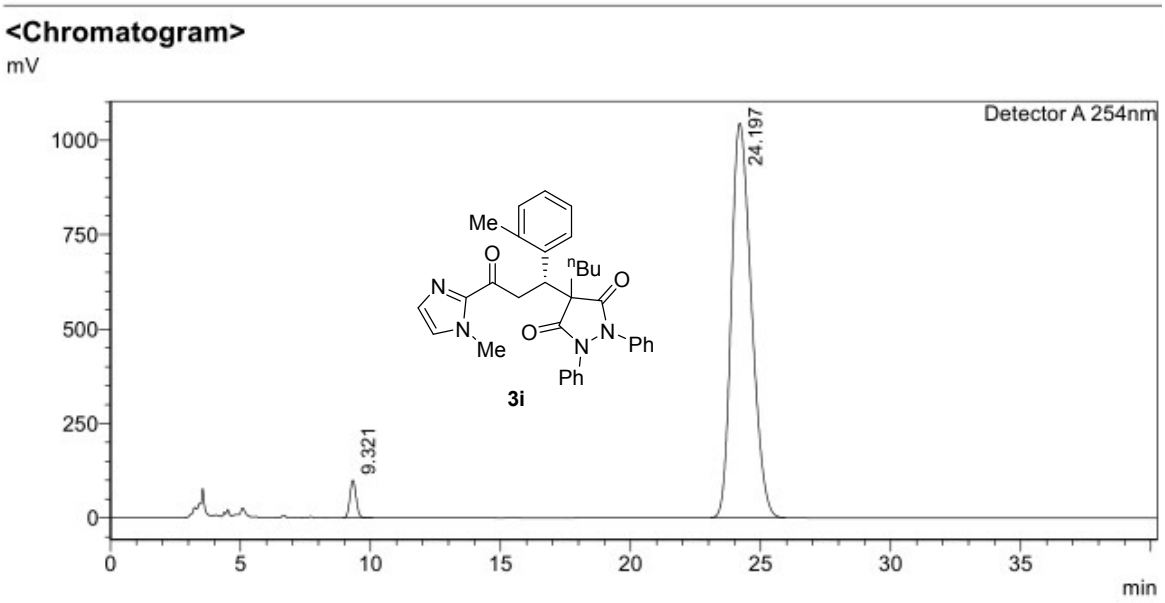


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.190	6250941	372437	50.155		M	
2	24.481	6212230	117409	49.845		M	
Total		12463171	489846				

Chiral **3i**:



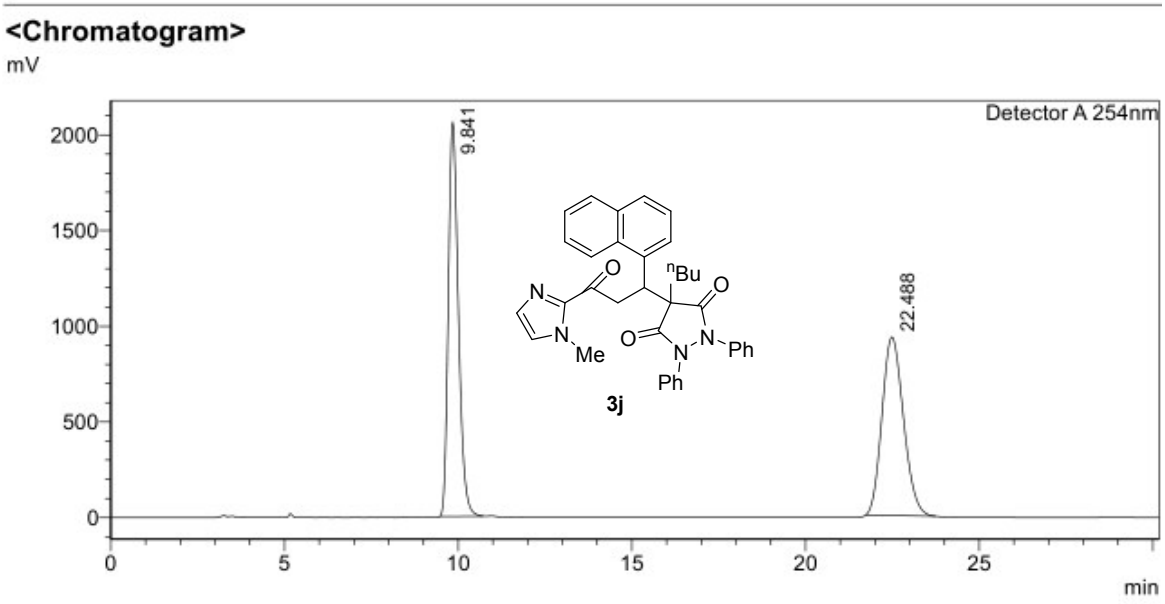
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.321	1671336	99729	2.898		M	
2	24.197	56004816	1044588	97.102		M	
Total		57676153	1144316				

HPLC traces of racemic **3i** and chiral **3i**. Area integration = 94.204% = 94% ee.

Racemic **3**j:

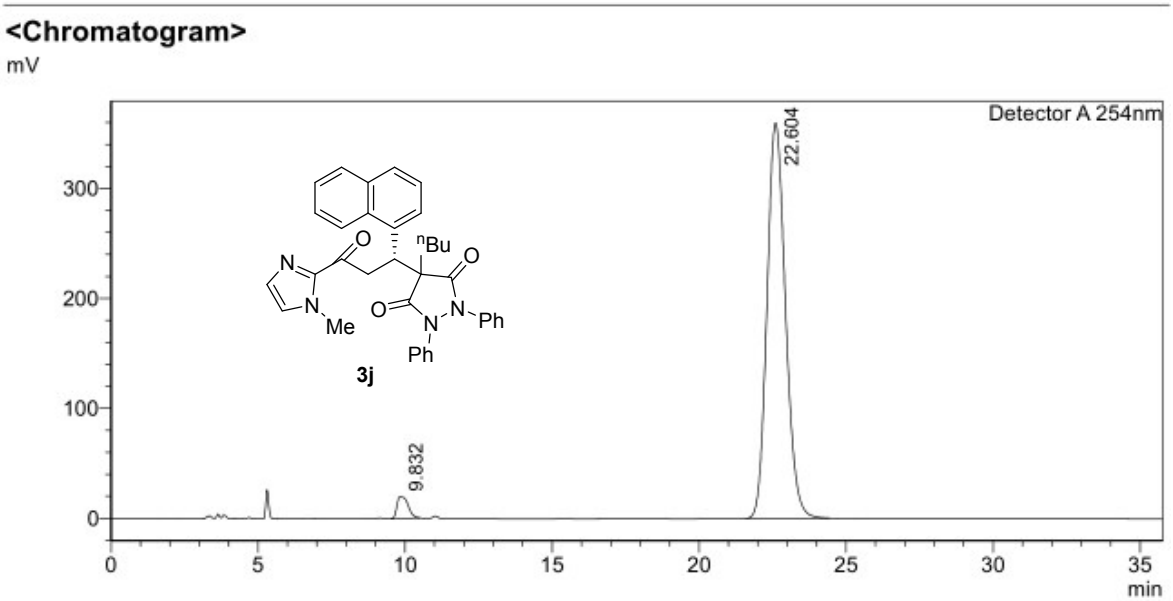


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.841	41430651	2057473	50.761		M	
2	22.488	40188641	932553	49.239		M	
Total		81619292	2990026				

Chiral **3j**:



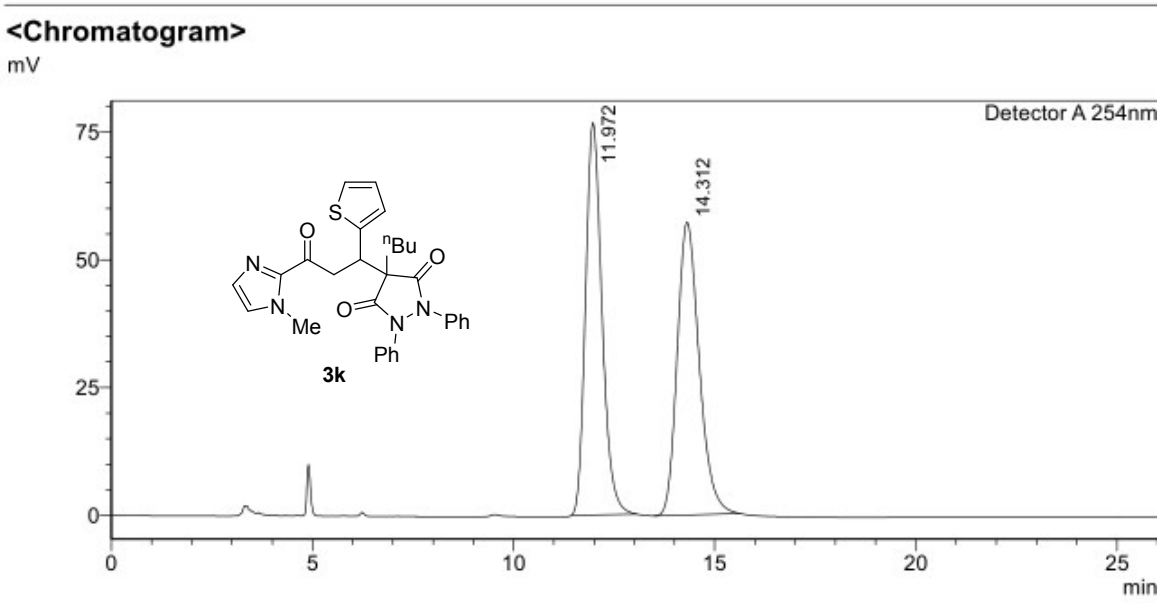
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.832	518923	19793	3.207		M	
2	22.604	15659804	359363	96.793		M	
Total		16178727	379156				

HPLC traces of racemic **3j** and chiral **3j**. Area integration = 93.586% = 94% ee.

Racemic **3**k:

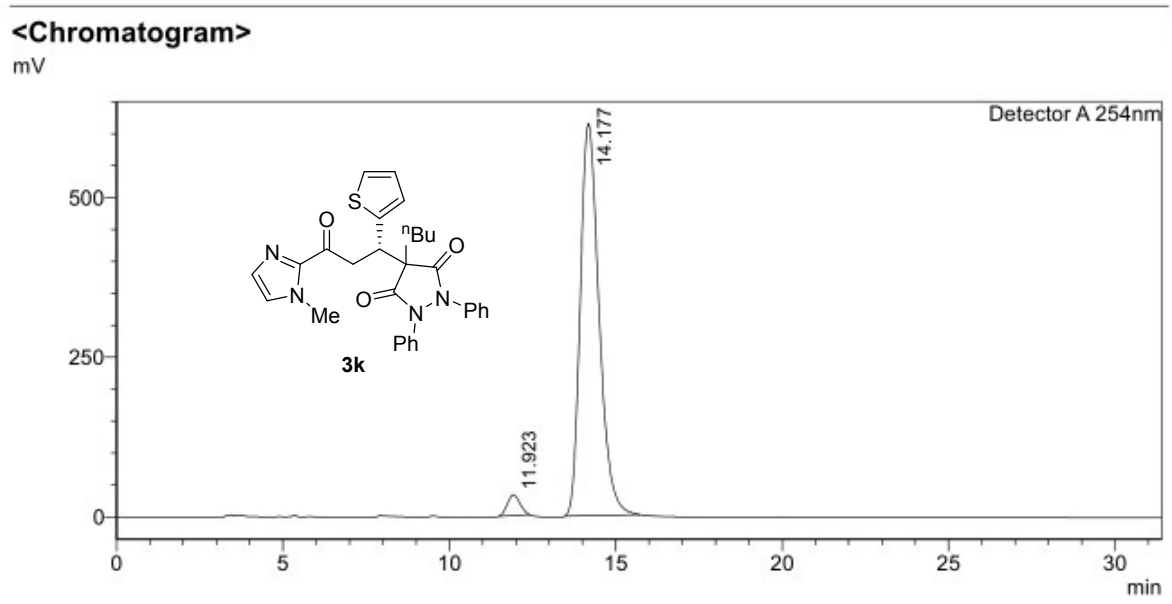


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.972	2177081	76658	50.057		M	
2	14.312	2172085	57210	49.943		M	
Total		4349166	133868				

Chiral **3k**:



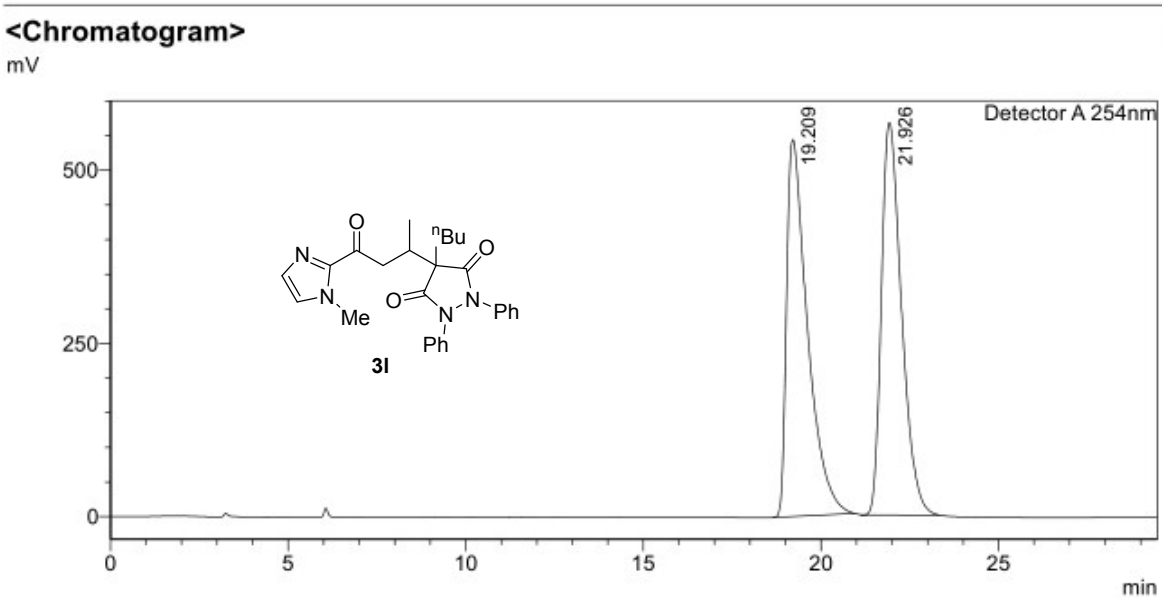
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.923	848880	32318	3.413		M	
2	14.177	24021762	614216	96.587		M	
Total		24870642	646534				

HPLC traces of racemic **3k** and chiral **3k**. Area integration = 93.174% = 93% ee.

Racemic **3l**:

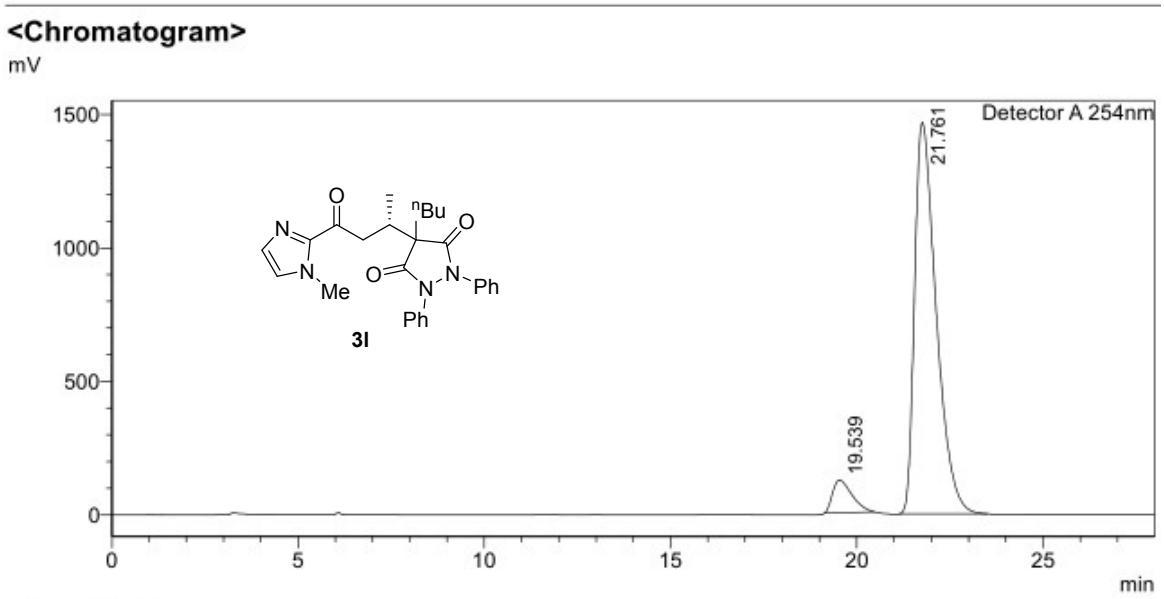


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	19.209	22241082	544144	49.950		M	
2	21.926	22285215	566003	50.050		M	
Total		44526297	1110146				

Chiral **3l**:



<Peak Table>

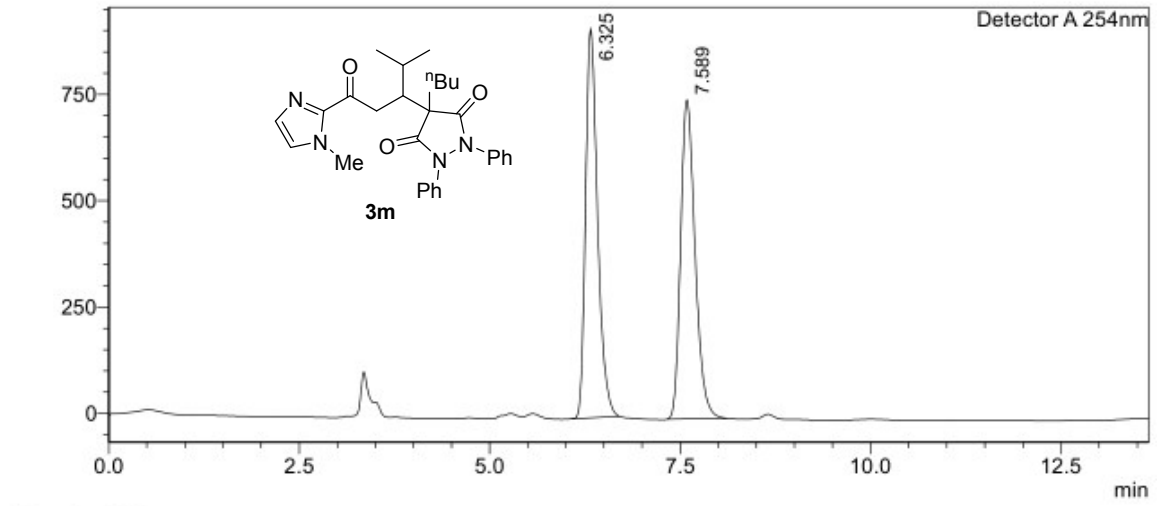
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	19.539	4417128	122147	6.954		M	
2	21.761	59104936	1466647	93.046		M	
Total		63522064	1588794				

HPLC traces of racemic **3l** and chiral **3l**. Area integration = 86.092% = 86% ee.

Racemic **3**m:

<Chromatogram>



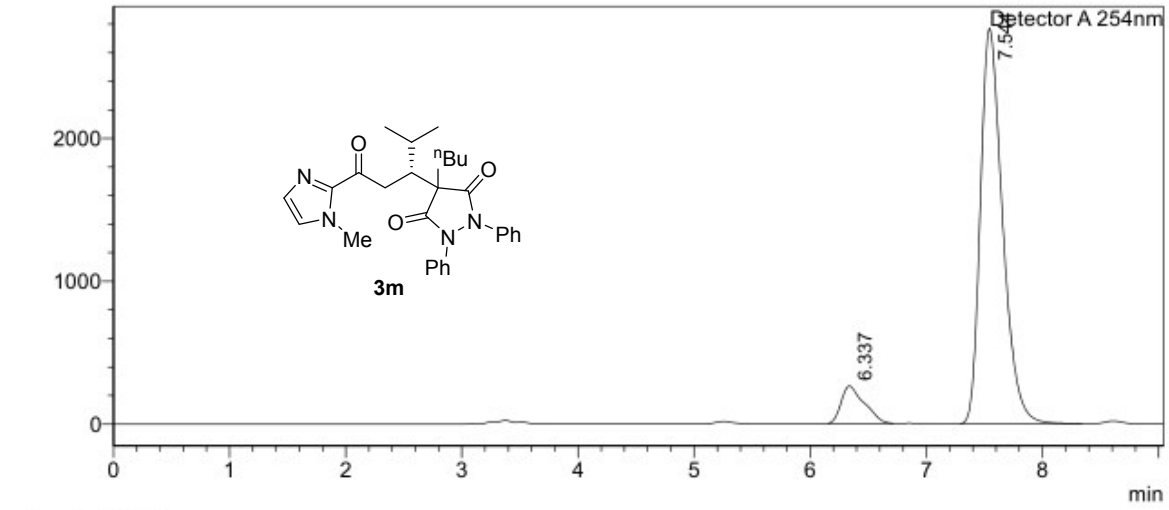
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.325	10003775	913482	50.268		M	
2	7.589	9896976	749932	49.732		M	
Total		19900752	1663414				

Chiral **3m**:

<Chromatogram>



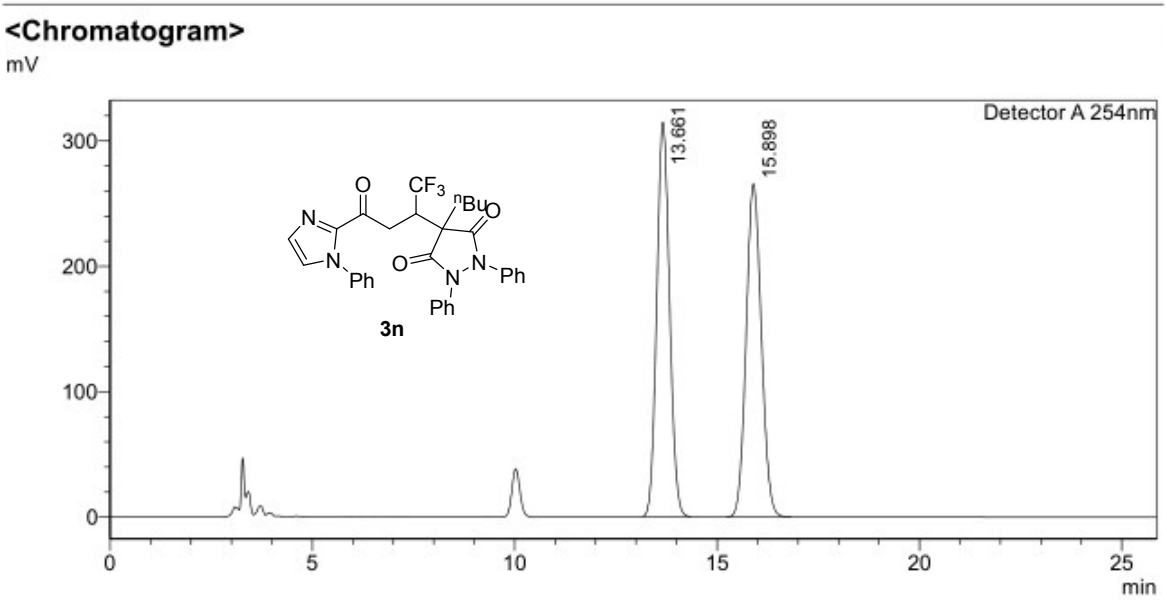
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.337	3609733	261533	8.954		M	
2	7.544	36706302	2765914	91.046		M	
Total		40316035	3027447				

HPLC traces of racemic **3m** and chiral **3m**. Area integration = 82.092% = 82% ee.

Racemic **3**n:

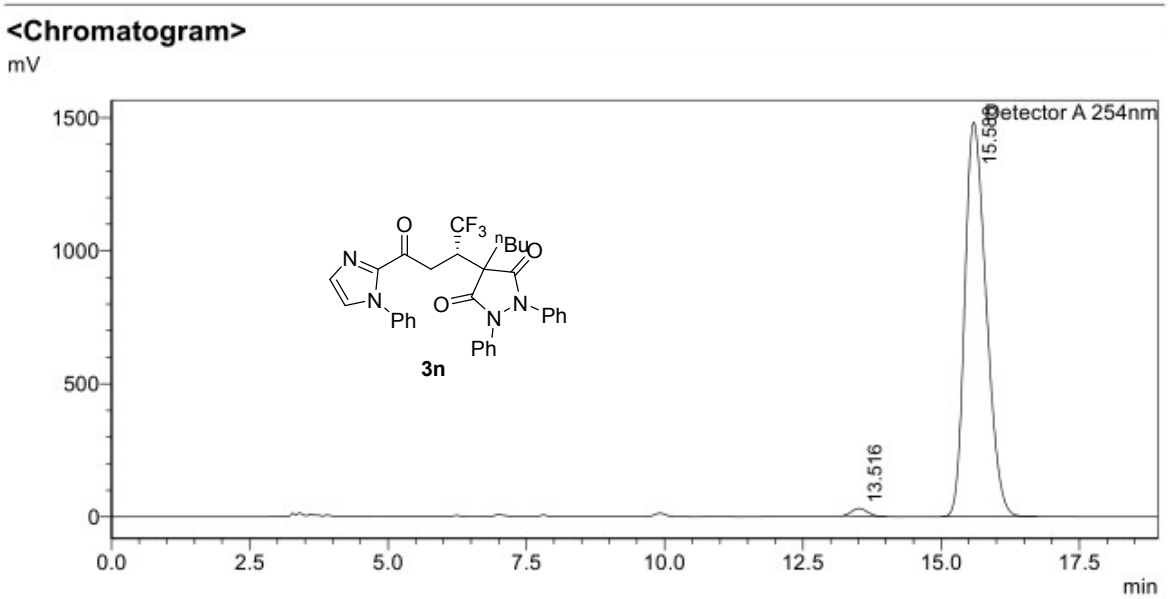


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.661	6913577	314439	49.892		M	
2	15.898	6943461	265568	50.108		M	
Total		13857038	580007				

Chiral **3n**:



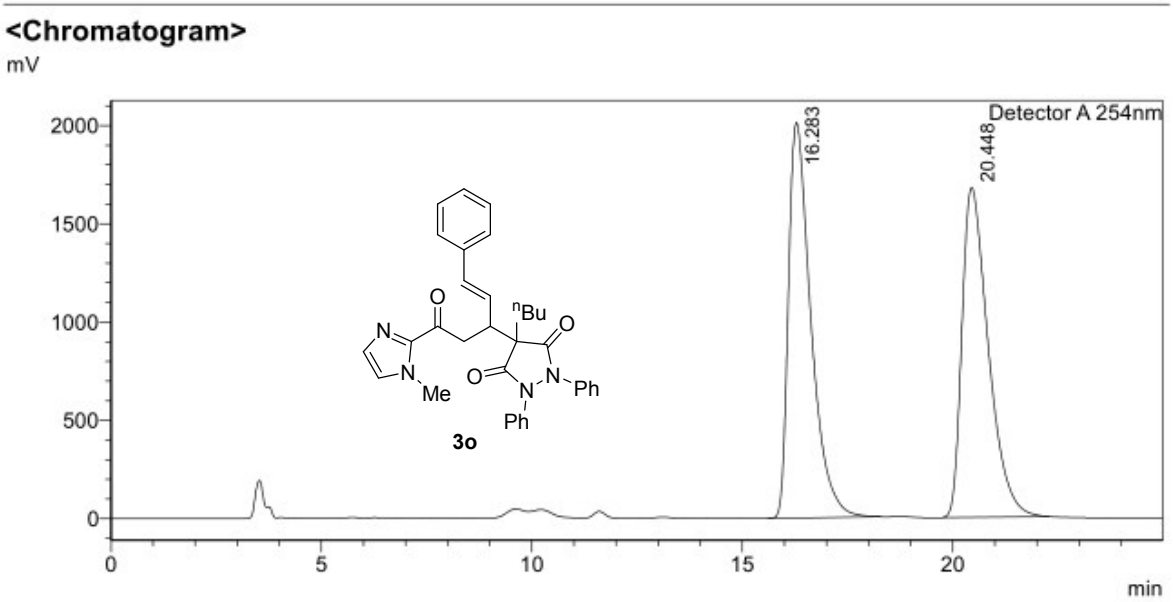
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.516	552913	28214	1.367		M	
2	15.588	39908896	1482834	98.633		M	
Total		40461808	1511049				

HPLC traces of racemic **3n** and chiral **3n**. Area integration = 97.266% = 97% ee.

Racemic **3**o:

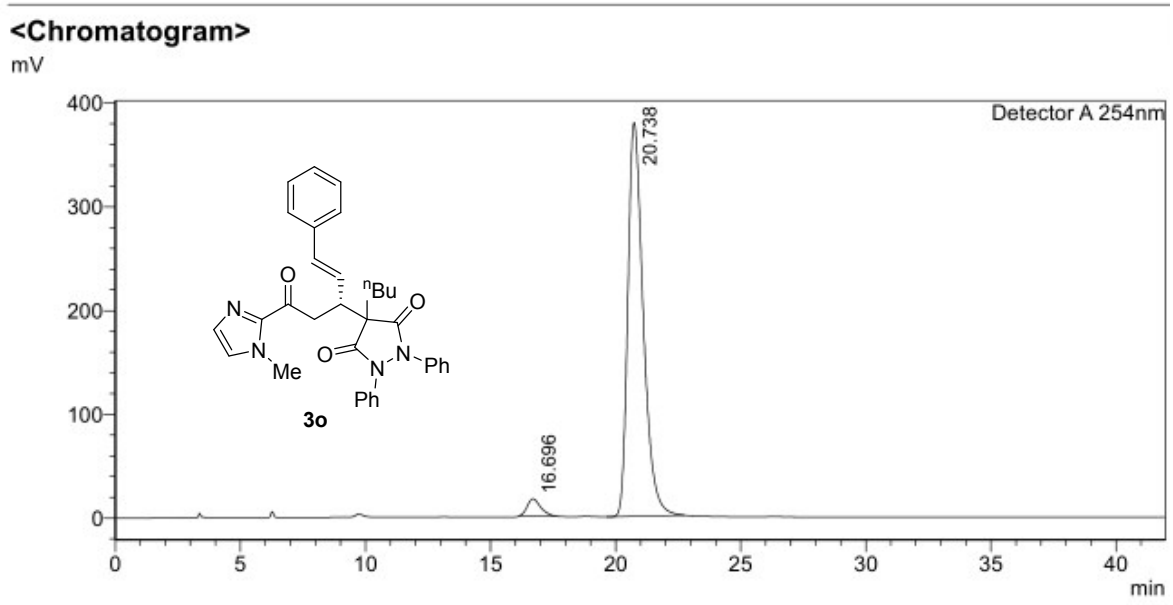


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.283	74579185	2012482	50.499		M	
2	20.448	73106279	1678474	49.501		M	
Total		147685464	3690955				

Chiral **3o**:



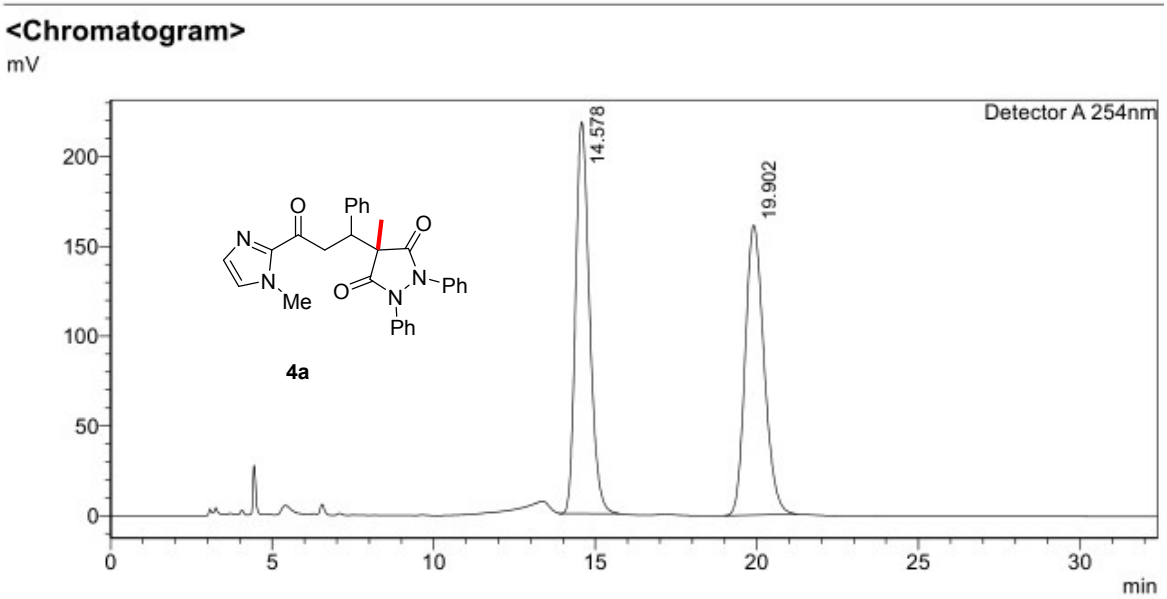
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.696	630402	16779	3.746		M	
2	20.738	16197695	379235	96.254		M	
Total		16828097	396014				

HPLC traces of racemic **3o** and chiral **3o**. Area integration = 92.508% = 93% ee.

Racemic **4a**:

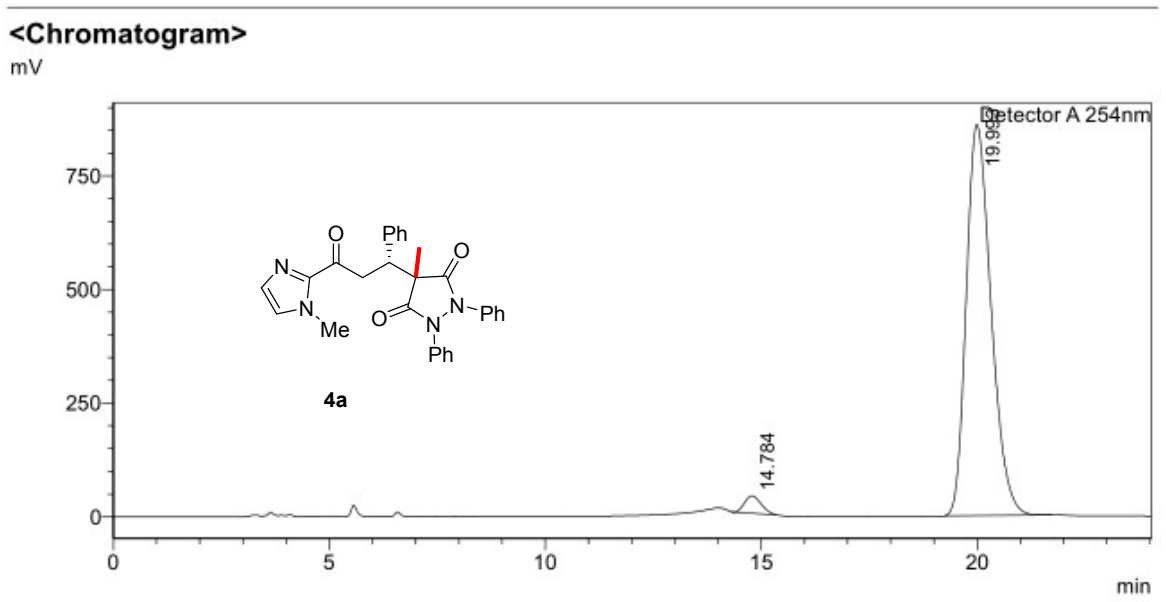


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.578	6528689	218101	50.003		M	
2	19.902	6527795	161458	49.997		M	
Total		13056484	379559				

Chiral **4a**:



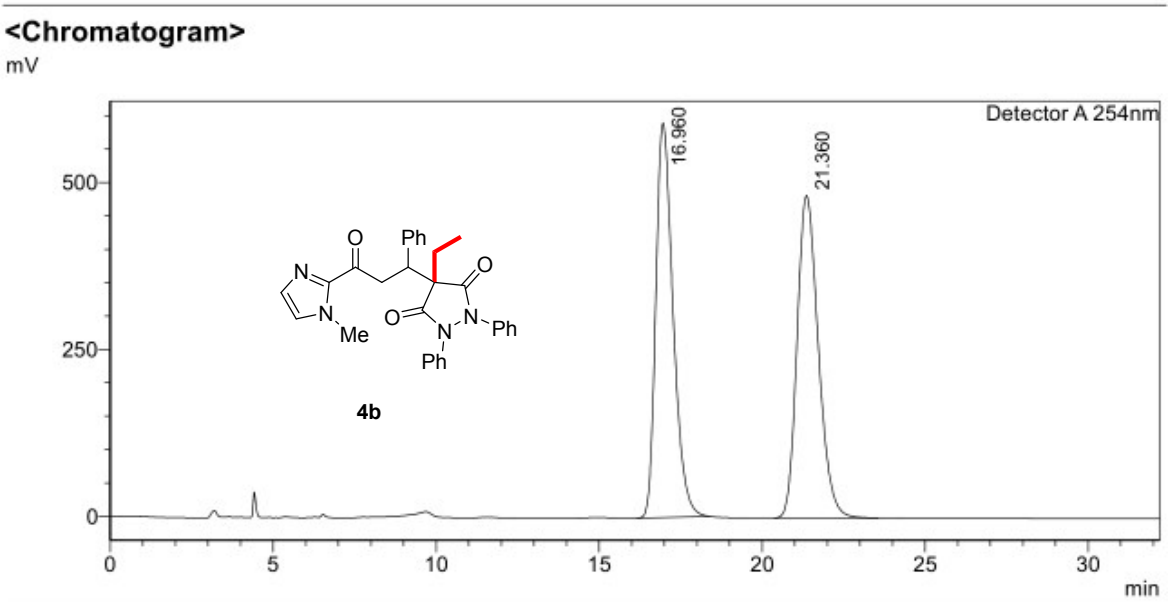
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.784	1012387	37915	2.865		M	
2	19.993	34330065	860317	97.135		M	
Total		35342452	898232				

HPLC traces of racemic **4a** and chiral **4a**. Area integration = 94.27% = 94% ee.

Racemic **4b**:

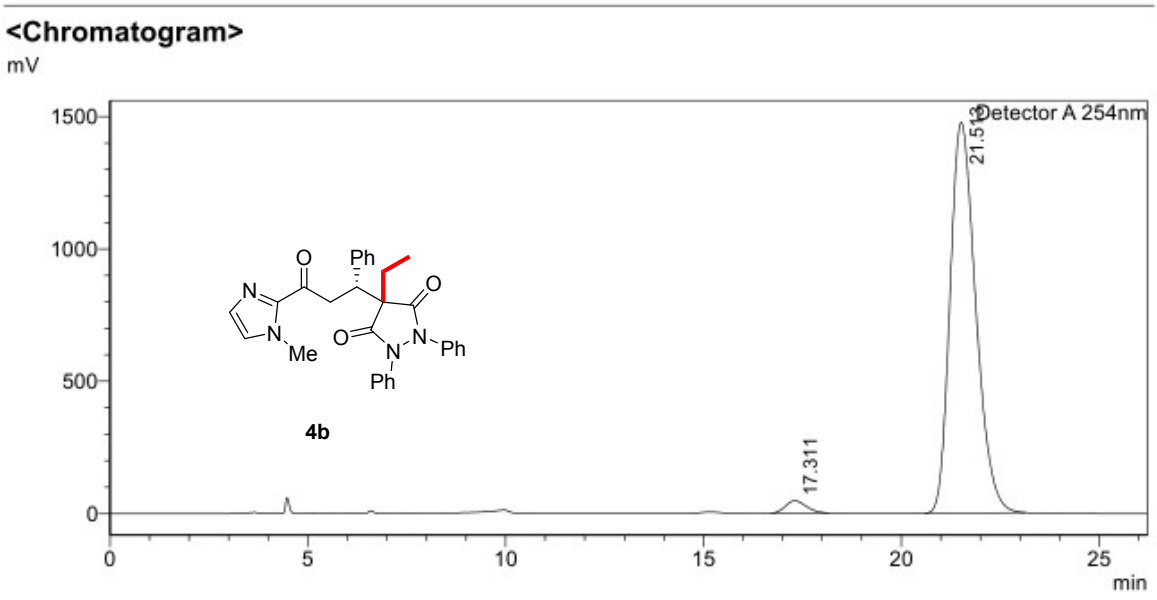


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.960	21719937	590749	49.815		M	
2	21.360	21880977	483034	50.185		M	
Total		43600914	1073784				

Chiral **4b**:



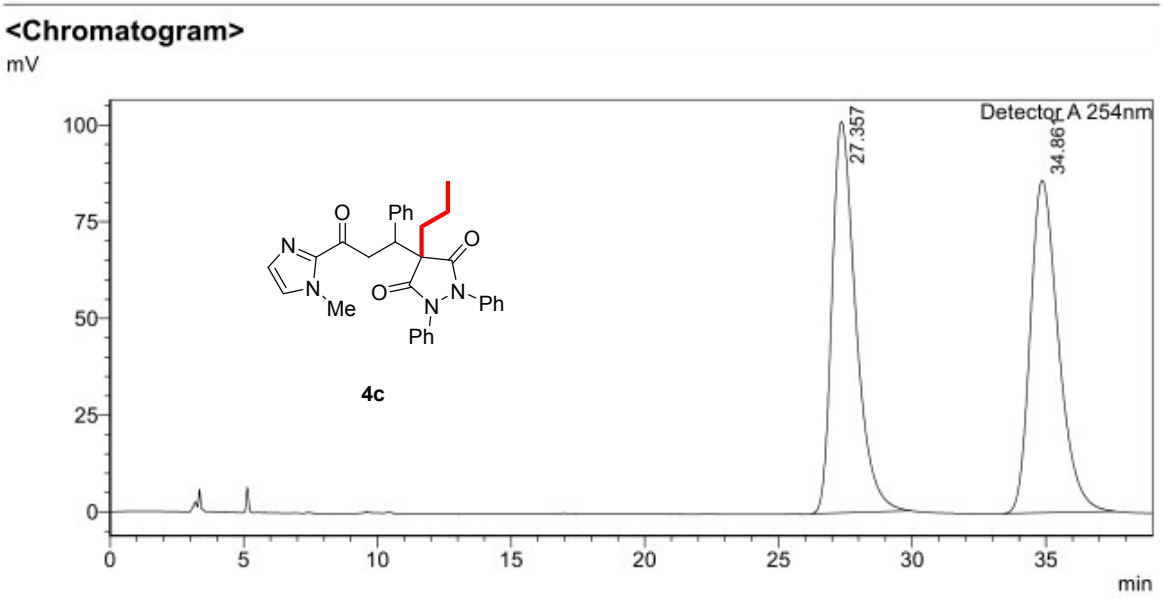
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	17.311	1719026	46693	2.514		M	
2	21.513	66661432	1476576	97.486		M	
Total		68380458	1523269				

HPLC traces of racemic **4b** and chiral **4b**. Area integration = 94.972% = 95% ee.

Racemic **4c**

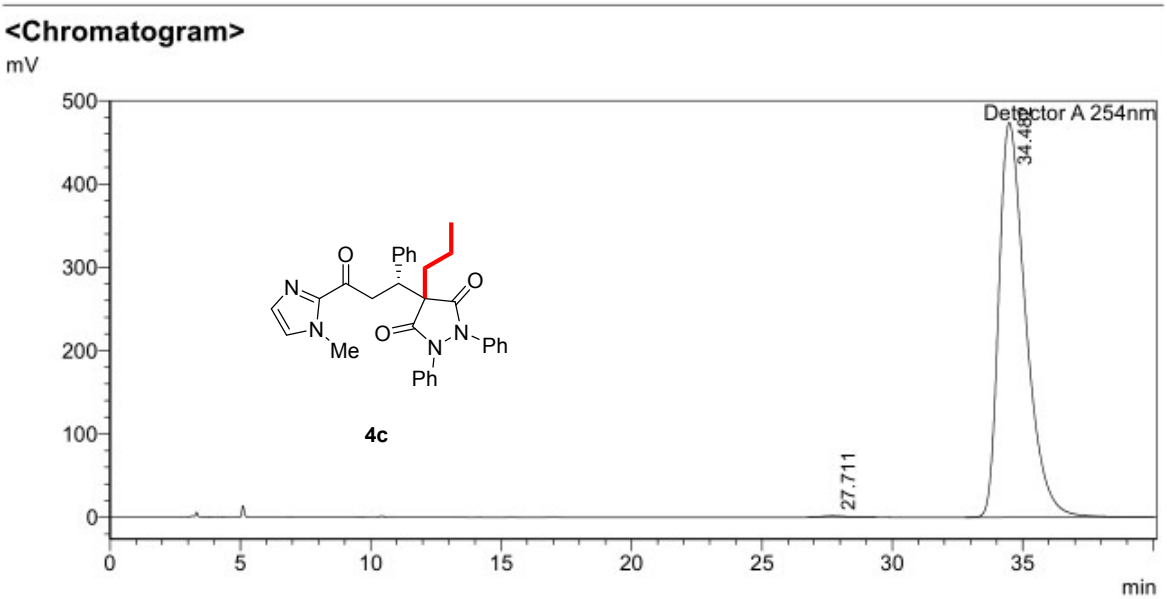


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	27.357	6235732	101096	49.839		M	
2	34.861	6276108	85944	50.161		M	
Total		12511840	187040				

Chiral **4c**:



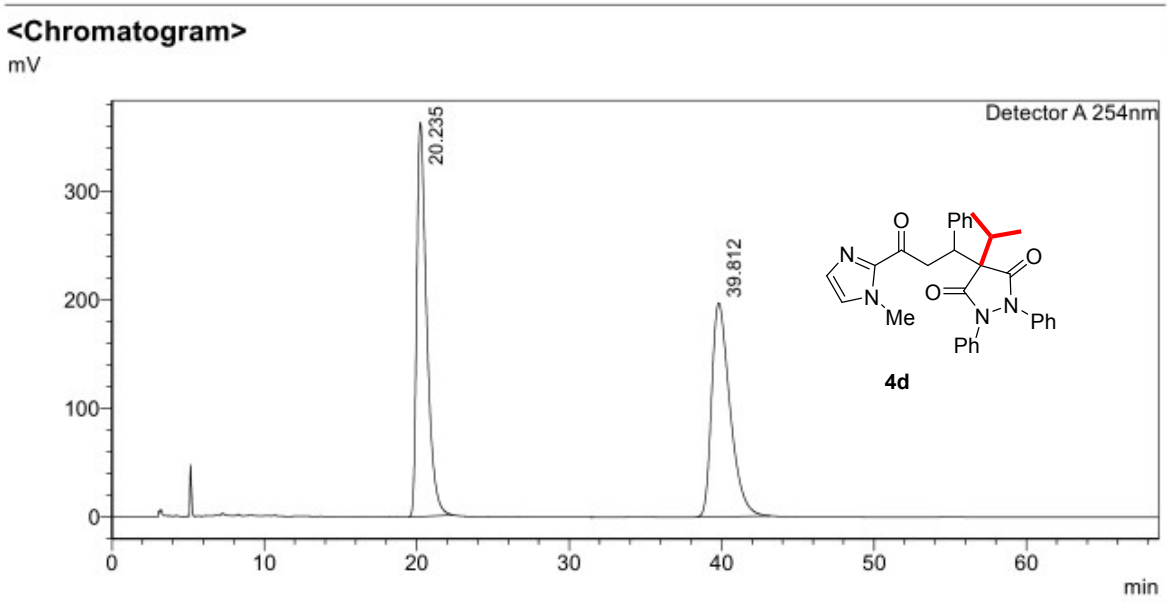
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	27.711	115144	1745	0.338		M	
2	34.482	33921877	473439	99.662		M	
Total		34037022	475185				

HPLC traces of racemic **4c** and chiral **4c**. Area integration = 99.324% > 99% ee.

Racemic **4d**

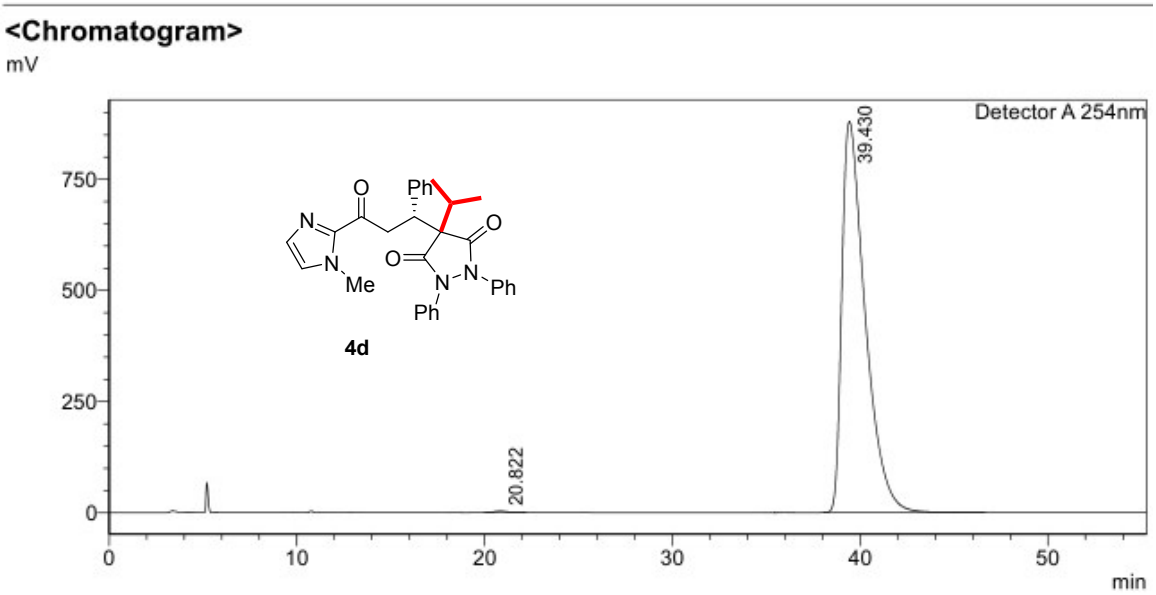


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	20.235	16494867	363133	50.070		M	
2	39.812	16448641	197084	49.930		M	
Total		32943508	560217				

Chiral **4d**:



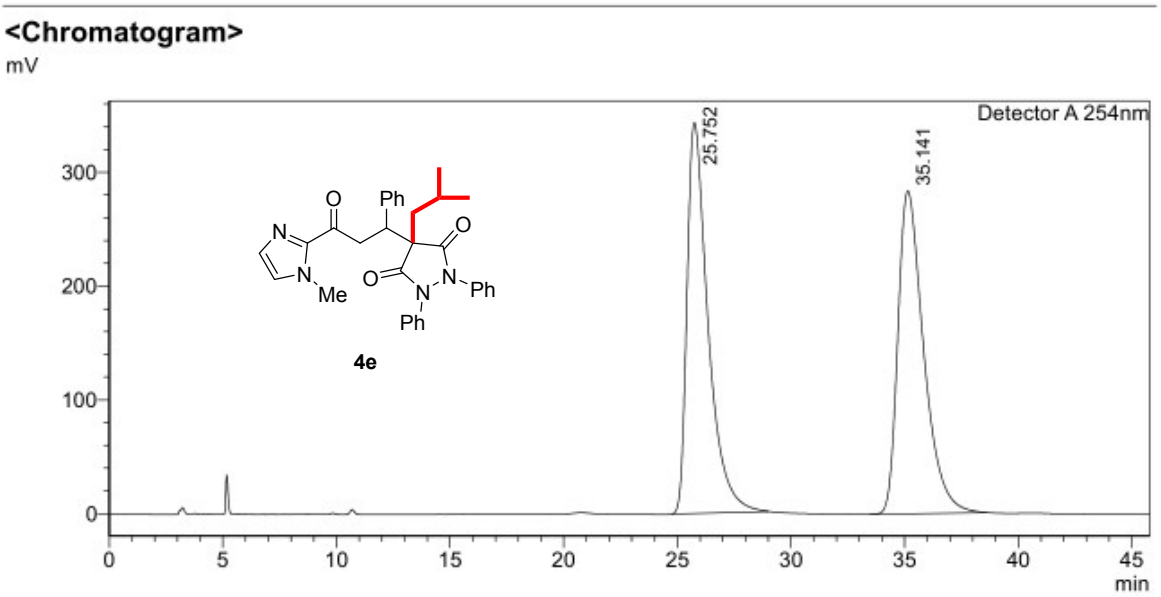
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	20.822	170697	3381	0.224		M	
2	39.430	75882817	879673	99.776		M	
Total		76053514	883054				

HPLC traces of racemic **4d** and chiral **4d**. Area integration = 99.552% > 99% ee.

Racemic **4e**

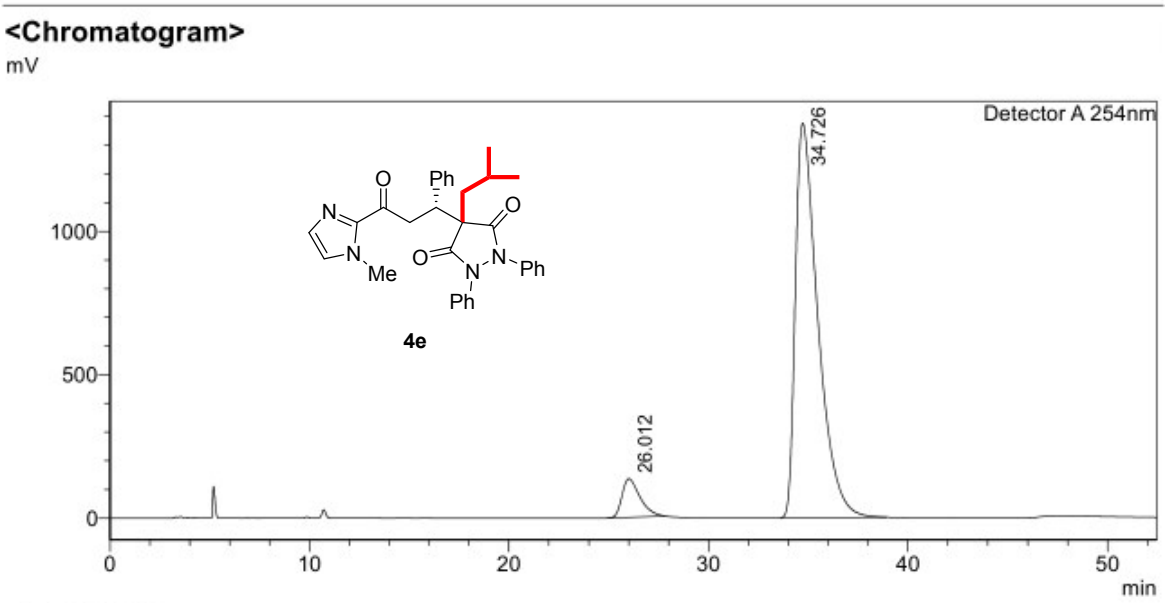


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	25.752	22059087	343435	49.668		M	
2	35.141	22353654	283666	50.332		M	
Total		44412741	627101				

Chiral **4e**:



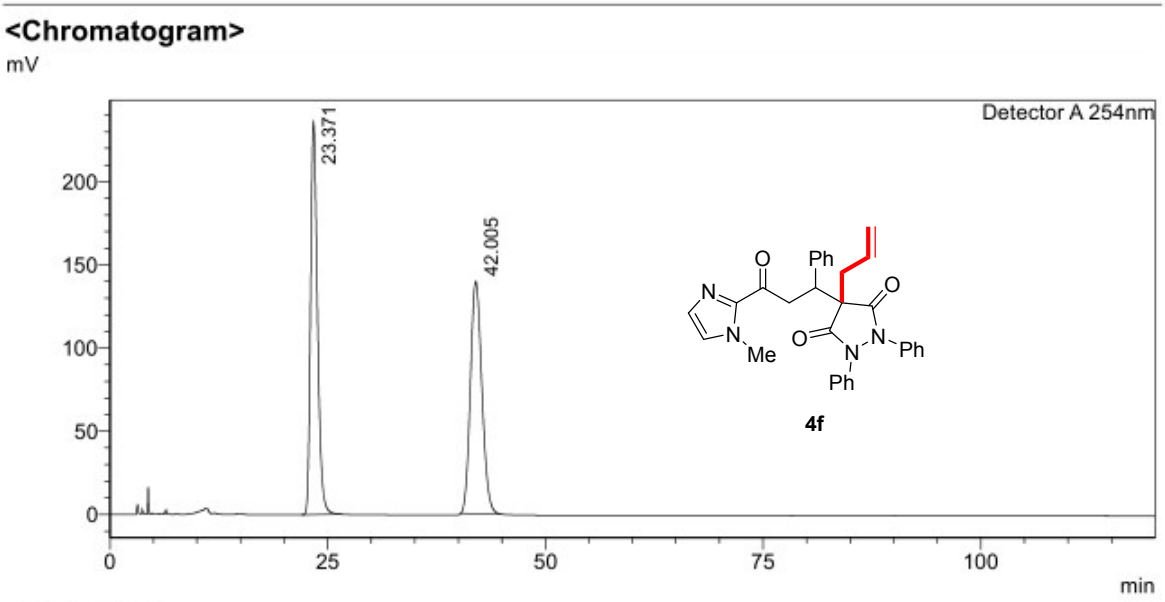
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	26.012	8473782	134549	7.280		M	
2	34.726	107916447	1375363	92.720		M	
Total		116390229	1509912				

HPLC traces of racemic **4e** and chiral **4e**. Area integration = 85.44% = 85% ee.

Racemic **4f**

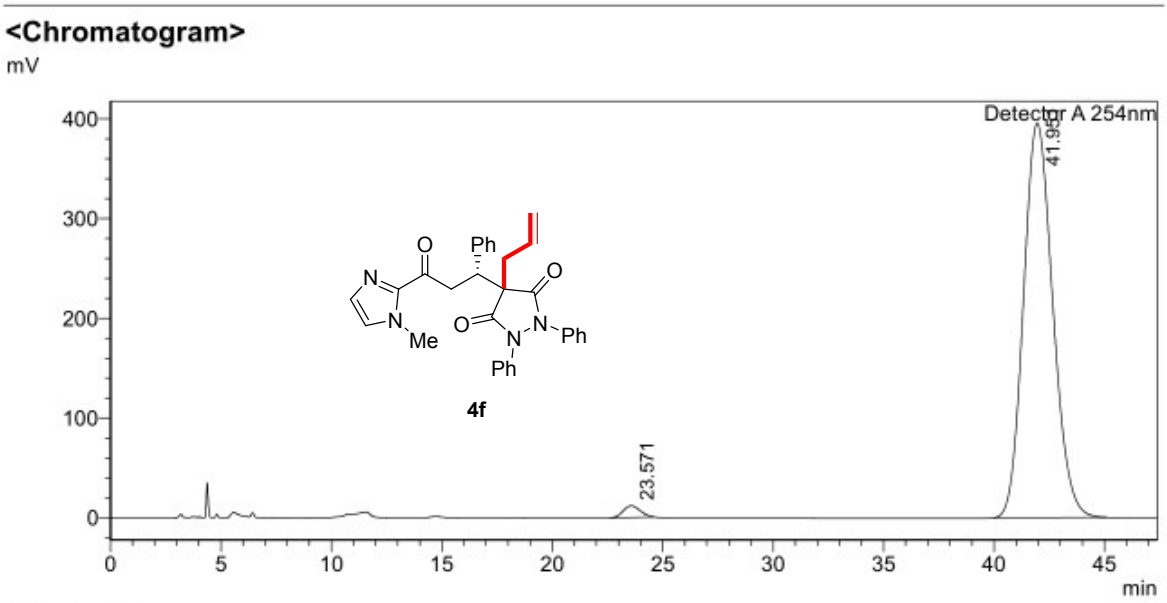


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	23.371	12963904	235941	50.338		M	
2	42.005	12790059	139562	49.662		M	
Total		25753963	375503				

Chiral **4f**:



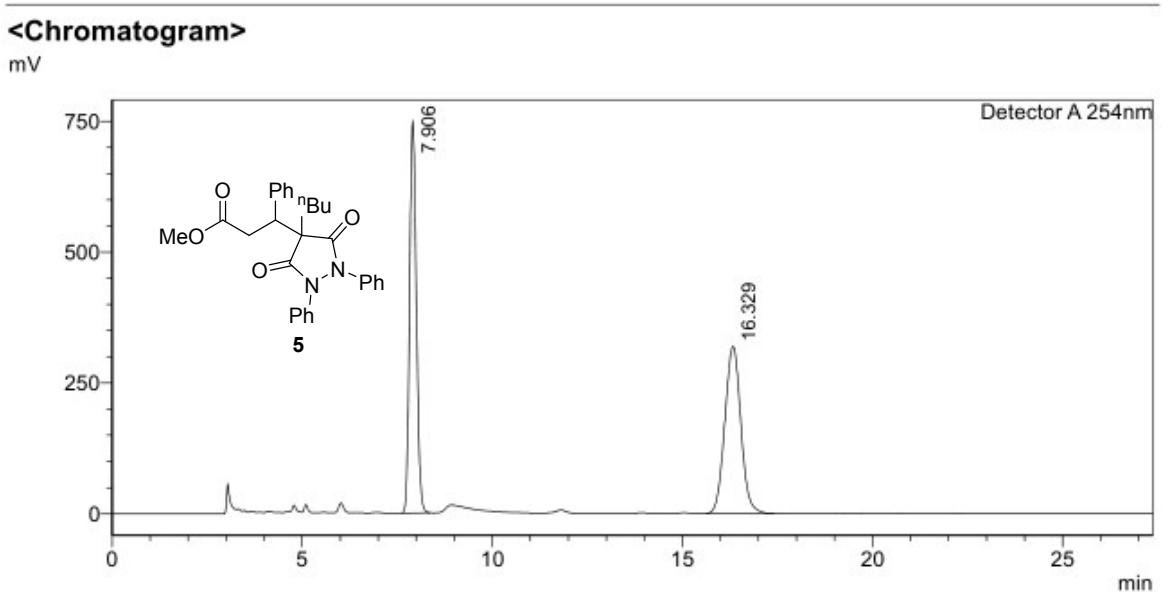
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	23.571	623236	11693	1.683		M	
2	41.951	36410336	395558	98.317		M	
Total		37033571	407251				

HPLC traces of racemic **4f** and chiral **4f**. Area integration = 96.634% = 97% ee.

Racemic **5a**:

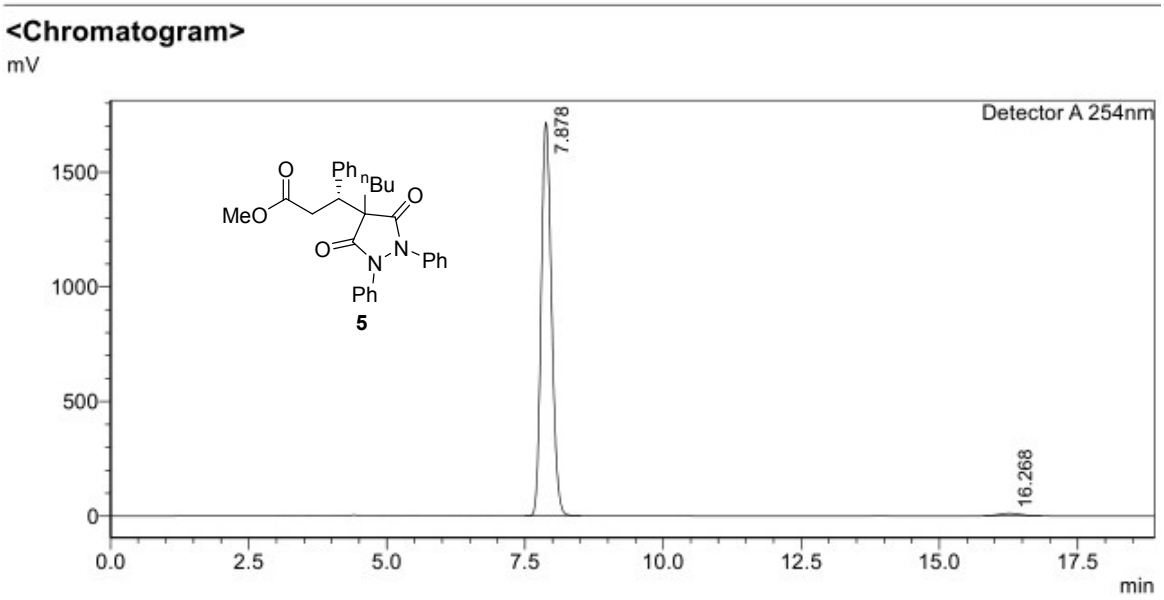


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.906	9194678	747250	49.533		M	
2	16.329	9368182	319198	50.467		M	
Total		18562860	1066447				

Chiral **5a**:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.878	22422282	1716281	98.589		M	
2	16.268	320931	11488	1.411		M	
Total		22743214	1727769				

HPLC traces of racemic **5a** and chiral **5a**. Area integration = 97.178% = 97% ee.